EXPERT REPORT OF DANIEL CICCARONE, MD, MPH

August 3, 2020

produced by morphine or heroin.[110] Several prescription opioids, e.g., oxycodone, hydromorphone, morphine, and fentanyl, have abuse potential that is similar to that of heroin.[111]

b. It has been reported that legitimate medical use of opioids for pain is a common precursor to misuse of those same drugs, thus providing the initial step in the transition from medical use of prescription opioids, to non-medical use, and for some, ultimately to heroin/FASH.[112]

c. A number of studies strongly support my opinion that prescription opioid misuse has been a recent "gateway" for initiation of heroin use.[113]

d. Estimates of the proportion of individuals reporting misuse of prescription opioids prior to initiating heroin range, in different US locations, from 39 to 86 percent.[114]

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[110] Comer SD, Sullivan MA, Whittington RA, Vosburg SK, Kowalczyk WJ. Abuse liability of prescription opioids compared to heroin in morphine-maintained heroin abusers. Neuropsychopharmacology 2008;33:1179-1191

[111] Ternes JW, O'Brien CP. The opioids: abuse liability and treatments for dependence. Adv Alcohol Subst Abuse 1990;9:27-45 Comer SD, Sullivan MA, Whittington RA, Vosburg SK, Kowalczyk WJ. Abuse liability of prescription opioids compared to heroin in morphine-maintained heroin abusers. Neuropsychopharmacology 2008;33:1179-1191.

[112] McCabe, et al., Pediatrics 2017; 139:1-9.

[113] Cicero TJ, Ellis MS, Surratt HL, and Kurtz SP. 2014. The changing face of heroin use in the United States: A retrospective analysis of the past 50 years. JAMA Psychiatry 71(7); Compton et al, NEJM, 2016; Grau, L. E., Dasgupta, N., Harvey, A. P., Irwin, K., Givens, A., Kinzly, M. L., & Heimer, R. (2007). Illicit use of opioids: Is OxyContin a "gateway drug"? The American Journal on Addictions, 16(3), 166–173. http://dx.doi.org/10.1080/10550490701375293; Mars, S., Bourgois, P., Karandinos, G., Montero, F., & Ciccarone, D. (2014). "Every 'never' I ever said came true": Transitions from opioid pills to heroin injecting. International Journal of Drug Policy, 25(2), 257–266. http://dx.doi.org/10.1016/j.drugpo.2013.10.004

[114] Lankenau SE, Teti M, Silva K, Bloom JJ, Harocopos A, Treese M. Initiation into prescription opioid misuse amongst young injection drug users. Int J Drug Policy. 2012;23(1):37-44; Pollini RA, Banta-Green CJ, Cuevas-Mota J, Metzner M, Teshale E, Garfein RS. Problematic use of prescription-type opioids prior to heroin use among young heroin injectors. Subst Abuse

Muhuri et al. in a national study found that 79.5% of persons who recently began using heroin had used prescription opioids non-medically before initiating heroin use.[115] In a key retrospective analysis of almost 3,000 persons entering treatment for heroin use disorder, Cicero and colleagues found that the sub-type of opioid first use changed depending on when this use initiated. For current heroin users reporting first use in the 1960s, 80% reported starting with heroin; in contrast, 75% of those entering treatment for heroin use disorder in the 2000s reported that their first regular opioid was a prescription opioid.[116]

50. Our team, using in-depth qualitative methods, has explored heroin initiation during the wave one to wave two overlap. Our paper, *"Every 'Never' I Ever Said Came True": Transitions from opioid pills to heroin injecting*, led by HIT Co-Investigator Dr. Sarah Mars, has had a crucial impact on the field. Some important insights and observations from this paper:

a. We interviewed a spectrum of current heroin users in two cities, locations contrasting in demographics and heroin source supplies, between 2010 and 2012. The purpose of the study was to deeply examine ways in which heroin use was

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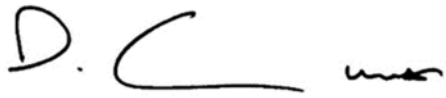
Rehabil 2011;2:173-180; Peavy KM, Banta-Green CJ, Kingston S, Hanrahan M, Merrill JO, Coffin PO. "Hooked on" prescription-type opiates prior to using heroin: results from a survey of syringe exchange clients. J Psychoactive Drugs 2012;44:259-265.

38. Mateu-Gelabert P, Guarino H, Jessell L, Teper A. Injection and sexual HIV/HCV risk behaviors associated with nonmedical use of prescription opioids among young adults in New York City. J Subst Abuse Treat 2015;48:13-20.

[115] Muhuri PK, Gfroerer JC, Davies C. Associations of nonmedical pain reliever use and initiation of heroin use in the United States. CBHSQ Data Review, 2013 https://img3.reoveme.com/m/25e062e91894208c.pdf (accessed June 20, 2020).

[116] Cicero TJ, Ellis MS, Surratt HL, and Kurtz SP. 2014. The changing face of heroin use in the United States: A retrospective analysis of the past 50 years. JAMA Psychiatry 71(7).

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.



Dated: August 3, 2020

Daniel Ciccarone, MD, MPH

EXPERT REPORT OF KATHERINE KEYES, PHD

August 3, 2020

terms of geographic variation in supply as well as year-to-year variation, in both observational and quasi-experimental studies, providing an evidence base that supports this opinion that supply and availability of opioids caused an increase in the rate of prescription opioid overdose.

9. Prescription opioids cause accelerated and increased risk of harm when used in conjunction with other drugs such as other opioids, benzodiazepines, stimulants, and alcohol. When multiple drugs are listed as part of the contributing causes of death in an overdose death, the preponderance of evidence indicates that certain combinations of drugs, especially those that include opioids, are associated with multiplicative increases in risk of death; that is, without the prescription opioid, the individual would not have died when and how they did. Thus, multiple drugs present in a toxicology report are likely indicative of drug-drug interactions for which prescription opioids are attributed as a cause when listed as per the current available evidence in epidemiological and toxicological sciences. For these reasons, CDC and other authoritative sources correctly report overdose deaths that include prescription opioids as prescription-opioid deaths, even when additional drugs are identified.[2]

10. In the United States, almost 47,000 people in the US died of a drug overdose in 2018 for an opioid-involved overdose death rate of 14.6 per 100,000,[3] an almost 6-fold increase since 1999.[4–6] The beginning of the opioid crisis was marked by a rise in prescription opioid overdose deaths. West Virginia has the highest rate of opioid overdose in the nation, and among counties that report overdose rates, Cabell County has been among top ten counties with the highest overdose rate for the last four out of four years. In 2018, the last year of data available, I estimate that the prevalence of extra-medical opioid use is approximately 8-9% in the general population, underlying more than 100 people who have died due to opioid overdose. Approximately three quarters of those who use extra-medically, and those fatally injured by opioids, began their opioid use with prescription opioids.

11. In addition to fatal overdose, other consequences to the Cabell Huntington community affected by opioid oversupply include emergency department visits for overdose, increased burden in the treatment and chemical dependency provider system, opioid use disorder and opioid use among both adults and adolescents, and neonatal abstinence syndrome (NAS).

12. Prescription opioid and other opioid mortality disproportionately affected economically deprived areas; however, the available evidence indicates that economic conditions played a relatively small part in increased opioid-related morbidity and mortality. The driving force in increasing opioid-related morbidity and mortality was, and continues to be, access to and wide-spread availability of opioids.

13. Compared with other commonly used pain relievers, such as non-steroidal anti-inflammatory drugs (NSAIDs), the adverse health and addiction consequences are substantially and significantly greater from opioids than from NSAIDs, including for cardiovascular events, fractures, and falls, as well as poisoning and overdose.

To summarize, there is compelling evidence of harm from the oversupply of prescription opioids, both for medical users, and to non-medical users because of diversion. The Cabell Huntington community has experienced a high burden of harm due to opioids. These harms include opioid use disorders and overdose; these harms are greater than those associated with other pain relief drugs, and are causally related to additional harms from opioids including transition to heroin addiction.

III. METHODOLOGY

A. Definitions of methodological and substantive terms

Before detailing the scientific evidence that underlies my opinions, it is useful to describe a set of terms that I will be using throughout the report.

1. *The Cabell Huntington Community*. Throughout this report I will be describing epidemiological trends that relate to the county of Cabell in West Virginia, as well as the City of Huntington. I will note

specifically where data that are referred to are drawn from, but the inference for the report should be understood to relate to the overall community that is included in Cabell County and the City of Huntington.

2. *Prescription opioids*. Drugs approved for medical use in the United States for the control of moderate to severe pain that are either natural opiate analgesics derived from opium (morphine and codeine), semi-synthetic opioid analgesics (oxycodone, hydrocodone, hydromorphone, and oxymorphone), synthetic opioids (methadone), or synthetic opioid analgesics (e.g., tramadol and fentanyl).[7]

3. *Medical use of prescription opioids*. Medical use will refer to use of prescription opioids prescribed by a physician and used as directed by that physician exercising professional judgment acting within the scope of his or her license.

4. *Non-medical use of prescription opioids*. Non-medical use refers to both using prescription opioids more often or longer than prescribed, or use of prescription opioids without a prescription. These definitions are commonly used in large scale surveys of prescription opioid use in the population. For example, the National Survey on Drug Use and Health asks, "Have you ever, even once, used any prescription pain reliever in any way a doctor did not direct you to use it?" Examples given to respondents include use without a prescription, use in greater amounts, more often, or longer than prescribed, or use in any other way that a doctor did not direct. This question and similarly worded questions on other large-scale surveys are the commonly used assessment of non-medical prescription opioid use. Some reports also label this as "prescription opioid misuse"; however, I will use the term 'non-medical prescription opioid use' for consistency. Non-medical prescription opioid use is also referred to as '*opioid misuse'* in much of the literature, although definitions and measurement assessments differ in what is included as opioid misuse. For example, some measures of opioid misuse include using opioids for euphoria, or for the experience or feeling that using opioids caused, which could conflate some medical and non-medical reasons for use.[8]

5. *Opioid misuse*. For the purposes of this report, opioid misuse is synonymous with "non-medical prescription opioid use", and refers to use of prescription opioids in ways other than prescribed, including taking more than prescribed, or using prescription opioids that were not prescribed by a physician. As noted above, however, throughout this report I will detail the definitions that studies use when using the term "misuse" to highlight variation in the definition in the literature, and will primarily rely on the term "non-medical use of prescription opioids" when discussing the literature and findings related to use of opioids that is outside the medical oversight and prescription of a physician.

6. *Tolerance and physical opioid dependence*. Individuals who use opioids can develop tolerance to the medication. Tolerance develops when the endogenous opioid system acclimates to the medication and more is needed to produce the desired effects. Dependence on opioids also occurs in medical uses of opioids, in which more opioids are needed to achieve the desired effects (tolerance) and when the cessation of opioids produces symptoms of withdrawal and craving for opioids. Physical opioid dependence can occur even at low doses, but is increased with dose and duration of use. Physical opioid dependence does not currently meet the criteria for opioid use disorder, with changes to the DSM in the most recent revision. Physical opioid dependence is expected even when opioids are used medically; yet physical opioid dependence is clinically challenging, and increases the risk for transition of patients to opioid use disorders and addiction.

7. *Opioid use disorders*. Opioid use disorder is a diagnosis in the DSM, as well as the International Classification of Disease (ICD). It is important to point out from the outset of this description that opioid use disorder is distinct from the physical opioid dependence (defined above) that would be expected to occur with repeated administration of opioids. Medical use of opioids would be expected to produce symptoms such as tolerance (needing more opioids to achieve the same effect) and withdrawal (uncomfortable and painful physical and psychological symptoms during cessation of opioids). However, opioid use disorders involve a maladaptive pattern of use from which there are serious consequences in domains of functioning. The fourth version of the DSM was published in 1994, and included two diagnoses that together comprised opioid use disorders: opioid abuse and opioid dependence. Opioid abuse was diagnosed if there was "a maladaptive pattern of use leading to clinically significant distress or impairment" as indexed by at least one of four symptoms in a 12-month period, including recurrent failure to fulfill major role obligations (e.g.,

Exhibits to this Report:
Attached as Exhibit A is a copy of my current curriculum vitae and a list of all publications authored by me in the past 10 years.
Attached as Exhibit B is a list of data or other information considered by me in forming the opinions expressed herein.
Attached as Exhibit C is a statement of my compensation for services performed in this case.
Attached as Exhibit D is a list of all cases in which I have testified as an expert at trial or by deposition during the past four years.

Pursuant to 28 U.S.C. Section 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed on: August 3, 2020

_____
Katherine Keyes

EXPERT REPORT, ANNA LEMBKE, M.D.

August 1, 2020

RELATING TO

Cabell County Commission and City of Huntington, West Virignia, (The Cabell Huntington Community) v. AmerisourceBergen Drug Corporation, Cardinal Health, Inc., and McKesson Corporation,

No. 1:17-op-45053-DAP and No. 1:17-op-45054

discontinuing opioids, including adverse medical consequences and serious risk of addiction and overdose death. Instead of helping patients with this goal, McKesson promoted maintaining and even increasing doses of Butrans: "In 2013, one of our commercial goals is to reduce discontinuation and improve patient adherence…. HCPs are initiating opioid-experienced patients inappropriately on the 5 mcg/hour when they should be initiated on the 10 mcg/hour. These factors are negatively impacting patient adherence, and Marketing would like to execute the McKesson Pharmacy Intervention Program in order to reduce the Butrans discontinuation rate."[193] This is another example of how Manufacturers and Distributors used 'improving patient adherence' as a proxy for boosting sales of a specific branded product.

6. No reliable scientific evidence shows that long-term opioid therapy is effective for chronic non-cancer pain.

a. Through the aforementioned methods, and by relying on flawed and industry-backed studies, the Pharmaceutical Opioid Industry encouraged and promoted several misconceptions concerning opioid use, including overstatement of benefits of long-term use for chronic pain. In fact, there is not, and has never been, reliable evidence that long-term opioid use improves pain or function to any clinically meaningful degree.

b. The best evidence available suggests that there is little or no improvement in pain or function for most patients on long-term opioid therapy. The Industry further claimed that the failure to prescribe opioids led to the "undertreatment of pain." Whether or not pain was undertreated does not change the fact that prescription opioids are an inappropriate method to address that concern, due to the absence of evidence of long-term benefit, and the strong evidence of unacceptable risk.[194] Patients often endorse ongoing subjective benefit from the opioid, not because it is treating

[193] *Id.*

[194] As stated in the NASEM 2017 Report, "The very real problems of underdiagnosis and undertreatment of pain are valid concerns, but *it would be a mistake to infer that greater utilization of opioids would ameliorate these problems*," due to the lack of evidence that opioids provide long-term benefits for chronic pain. NASEM Report (2017), fn. 42, above, at p. 51. (emphasis added).

underlying pain, but because it is relieving the pain of opioid withdrawal from the previous dose. Studies show that pain improves when patients on chronic high dose opioid therapy reduce their dose or come off opioids. Limiting opioid prescribing is good medicine, because it decreases exposure to a dangerous and potentially lethal drug, without compromising pain treatment.

c. Scientific evidence of prescription opioids' benefit for chronic pain has been repeatedly described as "weak," or "inconclusive." Randomized, placebo-controlled clinical trials, generally 12 weeks or less, were too brief to support claims of long-term benefit, and non-randomized trials do not provide reliable evidence of efficacy. Such evidence was inadequate to support the widespread use of the drugs and the risks they imposed. Even the 2009 Guidelines promulgated by advocacy groups funded by the Pharmaceutical Opioid Industry admitted that evidence regarding chronic opioid therapy was "insufficient to assess effects on health outcomes."[195] Twelve-week studies of opioids are insufficient to assess their risks and benefits, for the following reasons:

i. Prescription opioids differ from other pain medications in important ways. In addition to providing acute pain relief, opioids also have unintended psychotropic effects (improved mood, increased energy, decreased anxiety), which make them more likely to be reinforcing and to lead to addiction. Patients with chronic pain can find opioids reinforcing, independent of whether they provide pain relief.[196] Although addiction to opioid painkillers can occur quickly in some individuals, for others, addiction may take weeks, months, or years to manifest, and duration of exposure is the most significant risk factor for addiction (*see* discussion of Edlund study, above). Hence, a true assessment of the risks of highly addictive drugs like opioid pain relievers (the molecular equivalent of heroin) requires a longer period of study than 12 weeks.

[195] Chou R. Clinical Guidelines for the use of chronic opioid therapy in chronic noncancer pain. *Journal of Pain.* 2009;10(2):113-130 at p. 130.e5.

[196] Matthias M, Donaldson MT, Jensen AC, Krebs EE. "I was a little surprised": Qualitative Insights from Patients Enrolled in a 12-Month Trial Comparing Opioids to Non-Opioid Medications for Chronic Musculoskeletal Pain. *J Pain*. 2018: 1-9, at p. 1.

ii. According to a study of combat injury victims among military personnel, 6.8% developed an opioid addiction after a short-term prescription of opioids (within a 7-day discharge window). The median time to diagnosis of the opioid use disorder was 3 years.[197] The authors state that this was "the first study to show that persistent opioid use after trauma is associated with the development of clinically recognized opioid abuse years after the initial injury."[198] The long median time to diagnosis of opioid addiction reinforces the conclusion that industry-sponsored studies claiming a low risk of addiction are far too brief to provide reliable, real-world estimates of risk.[199]

iii. Naliboff *et al.*, in their two-arm, randomized, pragmatic clinical trial comparing stable dose to escalating dose of opioid medications among 135 patients at a VA clinic in Los Angeles, "carefully selected" as appropriate candidates for chronic opioid therapy, nevertheless discharged 27% of patients over the course of the study due to opioid misuse/noncompliance.[200] Urine toxicology screens were included in the protocol.[201] The authors concluded, "Overall, this study confirms that even in carefully selected tertiary-care patients, substance misuse is a significant problem. Importantly, *40% of these misuse problems did not become apparent within the first 6 months, pointing out the need for studies of longer duration*."[202] (emphasis added). These data also support the need for ongoing monitoring for misuse and addiction in patients prescribed opioids long-term.

iv. There are serious and certain risks associated with long-term opioid therapy, including but not limited to tolerance, dependence, withdrawal, opioid induced hyperalgesia (increased pain caused by

[197] Beyer CA, Poltavskiy E, Walker LE *et. al.*, Persistent Opioid Use After Combat Injury and Subsequent Long-term Risk of Abuse: a retrospective cohort study. *Annals of Surgery*, 2019; 1-9, at p. 1.

[198] *Id.* at p. 3.

[199] See discussion of industry-sponsored studies of addiction risk at Section C.7, below.

[200] Naliboff BD, Wu SM, Schieffer B, *et al*. A randomized trial of 2 prescription strategies for opioid treatment of chronic nonmalignant pain. *J Pain*. 2011;12(2):288-296, at p. 288.

[201] *Id*. at p. 291.

[202] *Id*. at p. 295.

Exhibits to this Report:
Attached as Exhibit A is a copy of my current curriculum vitae and a list of all publications authored by me in the past 10 years.
Attached as Exhibit B is a list of data or other information considered by me in forming the opinions expressed herein.
Attached as Exhibit C is a statement of my compensation for services performed in this case.
Attached as Exhibit D is a list of all cases in which I have testified as an expert at trial or by deposition during the past four years.

Pursuant to 28 U.S.C. S 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed on: August 1, 2020

Anna Lembke, M.D.

Confidential

Report of Professor Thomas McGuire

Regarding Public Nuisance in the Cabell Huntington Community in West Virginia

Confidential

Table of Contents

I. Introduction

A. Qualifications

1. I am a Professor of Health Economics in the Department of Health Care Policy at Harvard Medical School, where I teach health economics in Harvard University's Ph.D. Program in Health Policy. In 2008, I received the Everett Mendelsohn Excellence in Mentoring Award from Harvard's Graduate School of Arts and Sciences. I received an A.B. degree from Princeton University and a Ph.D. degree in economics from Yale University.

2. I am a member of the National Academy of Medicine – formally, the Institute of Medicine (IOM) – and a Research Associate at the National Bureau of Economic Research. I served for ten years as an editor of the leading journal in the field of health economics, the *Journal of Health Economics*, and co-edited the *Handbook of Health Economics*, Volume II.

3. For more than 40 years I have conducted research on the economics of managed care, health insurance, health care payment systems, pharmaceutical drug pricing and procurement, the economics of health care disparities by race and ethnicity, and the economics of mental health policy. I have authored a series of published papers on the economics of drug prices, competition between branded and generic drug products, and insurance coverage for drugs.[1] I co-chaired four conferences on the Economics of Mental Health, sponsored by the National

[1] T.G. McGuire and S. Bauhoff, "Adoption of a Cost-Saving Innovation: Germany, UK and Simvastatin," in N. Klusen, F. Verheyen, and C. Wagner (eds.), *England and Germany in Europe – What Lessons Can We Learn from Each Other?* Baden-Baden, Germany: Nomos, 2011, pp. 11-26; E.R. Berndt, T.G. McGuire, and J.P. Newhouse, "A Primer on the Economics of Prescription Pharmaceutical Pricing in Health Insurance Markets," *Forum for Health Economics & Policy*, 14(2), 2011, Article 10; J. Glazer and T.G. McGuire, "A Welfare Measure of 'Offset Effects' in Health Insurance," *Journal of Public Economics*, 96, 2012, pp. 520-523; J. Glazer, H. Huskamp, and T.G. McGuire, "A Prescription for Drug Formulary Evaluation: An Application of Price Indexes," *Forum for Health Economics and Policy*, 15(2), 2012, Article 3; K. Drake, M. Starr, and T. McGuire, "Do 'Reverse Payment' Settlements Constitute an Anticompetitive Pay-for-Delay?" *International Journal of the Economics of Business*, 22(2), 2015, pp. 173-200; T. McGuire, *et al.*, "Resolving Reverse-Payment Settlements with the Smoking Gun of Stock Price Movements," *Iowa Law Review*, 101(4), 2016, pp. 1581-1599; K. Drake and T. McGuire, "Stock-Price Evidence for Anticompetitive Effects in the Nexium 'Reverse-Payment' Settlement," *Journal of Competition Law & Economics*, 12(4), 2016, pp. 735-747; R.S. Hartman, K.M. Drake, and T.G. McGuire, "Event Study Analysis in Cases with Multiple Brand-Generic Reverse-Payment Settlements," *International Journal of the Economics of Business*, 26(3), 2019, pp. 399-410; and K. Drake and T.G. McGuire, "Generic Entry Before the Agreed-Upon Date in Pharmaceutical Patent Settlements," working paper (https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3416632).

Institute of Mental Health. The National Institute of Drug Abuse has sponsored my research, including research for which I served as Principal Investigator. I have published papers on the cost of drug abuse, drug abuse in the workplace, financing drug abuse services, and related topics.[2] My research has been recognized by a number of awards, including the Victor Fuchs Lifetime Achievement Award for 2018, awarded by the American Society of Health Economics.[3]

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[2] T.G. McGuire and B. Shatkin, "Forecasting the Cost of Drug Abuse Treatment Coverage in Private Health Insurance," in Cartwright and Kaple (eds.) *Economic Costs, Cost Effectiveness, Financing and Community-Based Drug Treatment*, National Institute on Drug Abuse Research Monograph #113, 1991. D.C. Walsh, R.W. Hingston, and T.G. McGuire, "A Randomized Trial of Treatment Options for Alcohol-Abusing Workers," *New England Journal of Medicine*, 325, 1991, pp. 775-782. T.G. McGuire, C. Ruhm, and B. Shatkin, "Defining the Public Interest in Workplace Drug Abuse Policy," *National Institute on Drug Abuse Research Monograph*, 1992. T.G. McGuire and C. Ruhm, "Workplace Drug Abuse Policy," *Journal of Health Economics*, 12, 1993, pp. 19-38. R.G. Frank, T.G. McGuire, D.A. Regier, R. Manderscheid, and A. Woodward, "Paying for Mental Health and Substance Abuse Care," *Health Affairs*, 13(1), 1994, pp. 337-342. B.S. Arons, R.G. Frank, H.H. Goldman, T.G. McGuire, and S. Stephens, "Mental Health and Substance Abuse Coverage Under Health Reform," *Health Affairs*, 13(1), 1994, pp. 337-342. M. Commons, D. Hodgkin, T.G. McGuire, and M. Riordan, "Summaries of State Programs," in G. Denmead and B. Rouse (eds.), *Financing Drug Treatment Through State Programs*, Services Research Monograph No. 1, National Institute on Drug Abuse, 1994. M. Commons, D. Hodgkin, T.G. McGuire, and M. Riordan, "Paying For Drug Abuse Services in the Six New England States," in G. Denmead and B. Rouse (eds.) *Financing Drug Treatment Through State Programs*, Services Research Monograph No. 1, National Institute on Drug Abuse, 1994. R.G. Frank and T.G. McGuire, "Estimating the Costs of Mental Health and Substance Abuse Coverage for Public Policy," *Health Affairs*, 14(3), 1995, pp. 102-115. M. Commons, T.G. McGuire and M.H. Riordan, "Performance Contracting for Substance Abuse Treatment," *Health Services Research*, 32(5), 1997, pp. 631-650. M. Commons and T.G. McGuire, "Some Economics of Performance-Based Contracting for Substance-Abuse Services," in Egertson, Fox, and Leshner (eds.) *Treating Drug Abusers*, 1997, pp. 223-249. R.G. Frank and T.G. McGuire, "Savings from a Medicaid Carve-Out for Mental Health and Substance Abuse Services in Massachusetts," *Psychiatric Services*, 48(9), 1997, pp. 1147-1152. S.L. Ettner, R.G. Frank, T.G. McGuire, J.P. Newhouse, and E. Notman, "Risk Adjustment of Mental Health and Substance Abuse Payments," *Inquiry*, 35, 1998, pp. 223-239. R.G. Frank and T.G. McGuire, "Parity for Mental Health and Substance Abuse Care Under Managed Care," *The Journal of Mental Health Policy and Economics*, 1, 1998, pp. 153-159. M. Alegria, T.G. McGuire, M. Vera, G. Canino, D. Freeman, L. Matias, C. Albizu, H. Marin, and J. Calderon, "The Impact of Managed Care on the Use of Outpatient Mental Health and Substance Abuse Services in Puerto Rico, *Inquiry*, 38(4), 2001, pp. 381-965. M. Lu and T.G. McGuire, "The Productivity of Outpatient Treatment for Substance Abuse," *Journal of Human Resources*, 38(2), 2002, pp. 309-335. E. Fleming, H.-M. Lien, C.-T. Albert Ma, and T.G. McGuire, "Managed Care and Trends in Hospital Care for Mental health and Substance Abuse Treatment in Massachusetts: 1994-1997," *The Journal of Mental Health Policy and Economics*, 6, 2003, pp. 3-12. V. Ojeda and T.G. McGuire, "Gender and Racial/Ethnic Differences in Use of Outpatient Mental Health and Substance Use Services by Depressed Adults," *Psychiatric Quarterly*, 77(3), 2006, pp. 211-222. H.-M. Lien, M. Lu, C.-T. Albert Ma, and T.G. McGuire, "Progress and Compliance in Alcohol Abuse Treatment," *Journal of Health Economics*, 29 (2), 2009, pp. 213-225. E.J. Montz, T.J. Layton, A.B. Busch, R.P. Ellis, S.R. Rose, and T.G. McGuire, "Risk Adjustment Simulation: Health Plans May Have Incentives to Distort Mental Health and Substance Abuse Coverage," *Health Affairs*, 35(6), 2016, pp. 1022-1028. In addition, many of my papers refer to "mental health" or "behavioral health," terms which can include issues related to substance abuse. See my CV for other papers.

[3] I was the 1981 recipient of the Elizur Wright Award from the American Association of Risk and Insurance recognizing an "outstanding contribution to the literature on risk and insurance" for my book *Financing Psychotherapy*. In 1991, I received the Carl Taube Award from the American Public Health Association for "outstanding contributions to public health." Two of my jointly authored papers received "Best Paper of the Year"

In 2015, a jointly authored paper on reverse payment settlements in the drug industry received the Article of the Year Award from the *International Journal of the Economics of Business*.[4]

4. My litigation experience includes recent testimony at two drug industry antitrust trials.[5] In the *National MDL Opiate Litigation*, I have submitted testimony regarding the calculation of costs due to the opioid crisis and the analysis of public nuisance for the two Ohio bellwether counties (Summit and Cuyahoga).[6] For the State of Washington, I have also submitted written testimony regarding public nuisance.[7] I provided deposition testimony in the Ohio matter. Appendix A contains my CV and a list of my recent testimony. Appendix B lists the materials upon which I relied and/or considered for this Report. Appendix B also notes meetings and calls in which I participated that included Cabell County Huntington Community personnel and other experts in this matter. Appendix C contains supplementary material as noted in the body of this Report.

5. My rate of compensation in this matter is $850 per hour. I have been assisted in this matter by staff of Greylock McKinnon Associates working under my direction. I receive compensation from Greylock McKinnon Associates based on its collected staff billings in support of my work in this matter. My compensation does not depend upon the outcome of this litigation. I understand that discovery is ongoing. I reserve the right to update my analysis based on additional information.

awards in 2008, one from Academy Health for research on physician-patient interaction and one from the National Institute for Health Care Management for work on incentives in managed care plans. My paper on designing payment systems for private health insurance markets received the best paper of the year award in 2014 from the National Institute for Health Care Management.

[4] K. Drake, M. Starr, and T. McGuire, *op. cit.*

[5] *In re: Nexium (Esomeprazole) Antitrust Litigation*, United States District Court for the District of Massachusetts, MDL No. 2409, Civil Action No. 112-cv-11711, November 7 and 20, 2014 and *In re: Solodyn (Minocycline Hydrocholoride) Antitrust Litigation*, United States District Court for the District of Massachusetts, MDL No. 14-md-2503-DJC, March 26-27, 2018.

[6] *In re: National Prescription Opiate Litigation*, MDL No. 2804, Case No. 17-md-2804.

[7] *State of Washington v. Purdue Pharma L.P.; et al*., State of Washington, King County Superior Court, No. 17-2-25505-0 SEA.

B. Assignment

6. In their Corrected Joint and Third Amended Complaint, Cabell County and the City of Huntington (the Plaintiffs) allege:

> "Defendants have created and maintained a public nuisance by marketing, distributing, selling opioids, and/or exacerbating the flood of opioids into Plaintiffs' Community in ways that unreasonably interfere with the public health, welfare, and safety in Plaintiffs' Community."[8]

Throughout this Report, the "Cabell Huntington Community," or "Community" refers to the entire community of Cabell County and the City of Huntington, the Plaintiffs.[9]

7. In connection with the public nuisance claims raised by the Plaintiffs, I have been asked the following three questions:

- First, is there a framework within the area of applied microeconomics by which economists determine the existence of, and measure the extent of, what is known under the law as a "public nuisance?"
- Second, do I have an opinion to a reasonable degree of certainty in the area of applied microeconomics as to the magnitude of the economic costs, net of any benefits,[10] imposed in the Cabell Huntington Community by the sales and distribution of prescription opioid products in the Community?

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[8] Corrected Joint and Third Amended Complaint, *In re: National Prescription Opiate Litigation as it relates to Cabell County Commission and City of Huntington, West Virginia*, Case No. 1:17-op-45053-DAP (S.D. W.Va.) and Case No. 1:17-op-45054 (S.D. W.Va.), in the United States District Court for the Northern District of Ohio, Eastern Division, September 16, 2019 (hereafter Complaint), ¶ 1405.

[9] While the majority of the City of Huntington is in Cabell County, a small portion of it is in Wayne County. In 2018, the Wayne County portion of the City of Huntington counted 3,584 residents, representing approximately 7.8% of Huntington's total population of 45,758 residents. U.S. Census, City and Town Population Totals: 2010-2018, (https://www.census.gov/data/tables/time-series/demo/popest/2010s-total-cities-and-towns.html). I note in this Report where data only refer to Cabell County or the City of Huntington.

[10] The empirical framework I apply in this Report recognizes and quantifies not only costs in economic terms, but potential benefits in terms of effects on workforce participation. Consideration of costs net of any benefits reflects my understanding of a "balance test" of harms and value referred to in the Complaint at ¶ 1409 ("A balancing test to assist in determining the existence of a nuisance is whether the 'gravity of the harm outweighs the social value of the activity alleged to cause the harm.'").

- Further, do I have an opinion about whether the net costs imposed by the sales and distribution of prescription opioid products in the Community were of sufficient magnitude to constitute a public nuisance to the Community?

8. I have been asked to limit my analysis to the time period of 2006 to the present or until the most recent period for which data are available to make reliable estimates. The years for which data are generally available, at this point in time, are through 2018. Should additional data become available during the course of this litigation, and if I am asked to do so by counsel, I can update my analysis to include more recent data.

9. Because these questions are framed in the context of the legal term "public nuisance," I have been instructed by counsel to be guided by the following general definition of a public nuisance, as set forth in the Complaint:

> "A public nuisance is an act or condition that unlawfully operates to hurt or inconvenience an indefinite number of persons. The distinction between a public nuisance and a private nuisance is that the former affects the general public, and the latter injures one person or a limited number of persons only."[11]

10. Counsel have also referred me to the following definition from the Complaint, drawn from the Restatement (Second) of Torts:

> "A public nuisance is an unreasonable interference with a right common to the general public. Circumstances that may sustain a holding that an interference with a public right is unreasonable include the following:
>
> d. Whether the conduct involves a significant interference with the public health, the public safety, the public peace, the public comfort or the public convenience, or
>
> e. whether the conduct is proscribed by a statute, ordinance or administrative regulation, or

[11] Complaint, ¶ 1407 quoting *Sharon Steel Corp. v. City of Fairmont*, 334 S.E.2d 616, 620 (W. Va. 1985) (citing Restatement (Second) of Torts § 821B (1979)).

f. whether the conduct is of a continuing nature or has produced a permanent or long-lasting effect, and, as the actor knows or has reason to know, has a significant effect upon the public right."[12]

11. It is my understanding that Plaintiffs will prove that the Defendants have unlawfully sold and distributed prescription opioids in the Cabell Huntington Community. My Report addresses the economic harms imposed by the sales and distribution of prescription opioids from 2006 through 2018.

C. Summary of Opinions

12. First, I am of the opinion that there is a framework within the area of applied microeconomics by which economists can determine the existence of, and measure the extent of, what is known under the law as a "public nuisance." Within the field of economics there is a long tradition of analyzing the social consequences of private behaviors imposing harms on others, known as "negative externalities." This economic framework provides a natural parallel to the legal notion of public nuisance.[13]

13. Second, I am of the opinion that the economic costs incurred in the Cabell Huntington Community by the sales and distribution of prescription opioids far exceed any benefits. I estimate, to a reasonable degree of certainty in the area of applied microeconomics, that the magnitude of the net economic costs imposed by the sales and distribution of prescription opioid products over the period 2006-2018 is approximately $4.17 billion. The major components of these costs are listed in Table 1. Figure 1 depicts the relative shares of the harms making up the total. Most of the economic costs are attributed to death and disease, in accord with national studies on harms from the opioid epidemic. Other categories of cost, while large in absolute terms, as indicated by Table 1, are small relative to cost of death and disease. A point of emphasis throughout this Report is that standard economic methods underestimate the costs of harms in these "smaller" categories.

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[12] Complaint, ¶ 1408 (footnote omitted).

[13] K. Hylton frames the economics of a public nuisance as an externality. See K. Hylton, "The Economics of Public Nuisance Law and the New Enforcement Actions," *Supreme Court Economic Review*, 18(1), February 2010, pp. 43-76. Other references are contained in Section II below.

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Table 1
Monetary Value of the Net Economic Costs Attributed to the Sales and Distribution of Prescription Opioids in the Cabell Huntington Community 2006-2018

Harms Due to Sales & Distribution of Prescription Opioids	Valuation ($millions)
Excess deaths	$3,437.8
Excess morbidity	$501.3
Excess neonatal abstinence syndrome	$2.6
Excess crimes	$77.4
Excess property value loss	$92.3
Excess child maltreatment	$57.9
Total	**$4,169.2**

Sources: Tables 3, 5, 7, 8, 9, and Section III.E of this Report.

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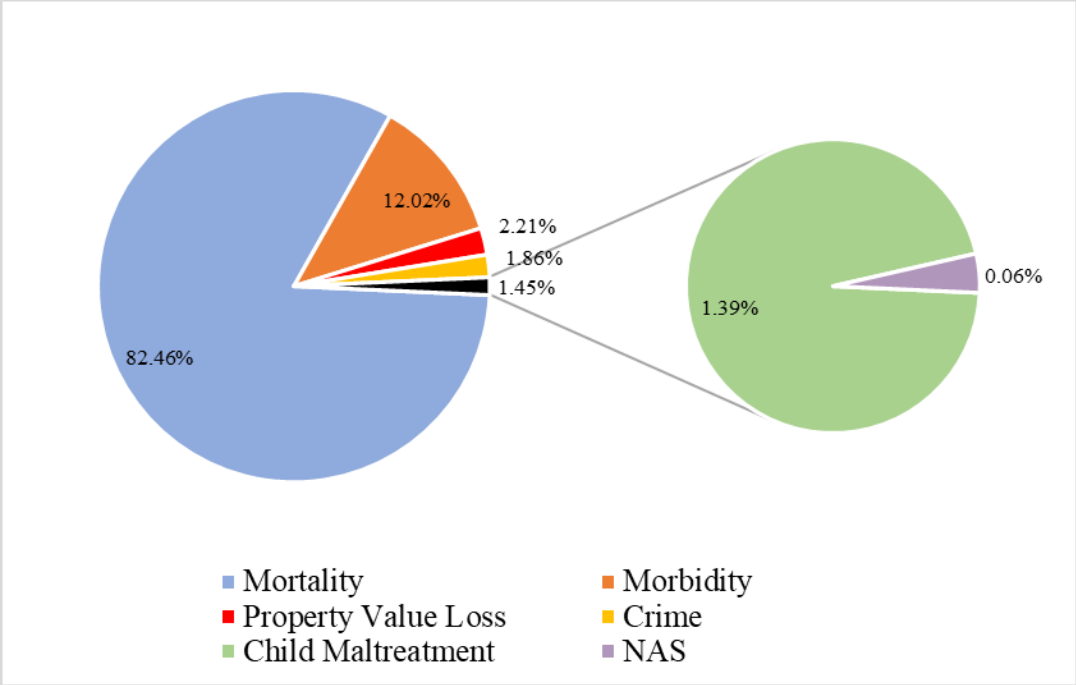
Figure 1
Percentage Value of Each Harm Attributed to the Sales and Distribution of Prescription Opioids in the Cabell Huntington Community 2006-2018



14. I have been instructed by counsel to report costs measured in dollars at the time they were incurred (as opposed to the equivalent costs in terms of dollars in 2020). A conversion to 2020 dollars can be done, if necessary, with standard methods. Doing so would substantially increase the dollar estimate of the net economic costs imposed.

15. Third, I conclude that sales and distribution of prescription opioid products imposed and continue to impose net economic costs of sufficient magnitude to constitute a public nuisance. As one indication, using the population of the Cabell Huntington Community in 2018 (96,619),[14] the costs reported in Table 1 amounted, over this 13-year period, to approximately $43 thousand per person in the Community.

[14] This is the sum of the population of Cabell County, and the portion of the City of Huntington located in Wayne County. U.S. Census, Cabell County Population by Characteristics, 2010-2019 (https://www.census.gov/data/tables/time-series/demo/popest/2010s-counties-detail.html). The population of Huntington, Wayne County is 3,584.

16. Fourth, my monetary estimates of the economic costs from the sales and distribution of prescription opioids underestimate the harm suffered by the Cabell Huntington Community. The inflow of prescription opioids injures Community residents in countless ways, not limited to a rash of fatal and non-fatal opioid overdoses, the taxing of the local health care system and social safety net, which are aimed at abating suffering from the numerous consequences of addiction, and an unprecedented number of babies born with neonatal abstinence syndrome. Standard economic approaches using available data fail to capture the full long-term devastation – damage to families and children, risk of crime, loss of employment, among other harms – that has befallen the Cabell Huntington Community and its residents due to the sales and distribution of prescription opioids. Because the long-term effects of the opioid epidemic are at present unknown, and because some harms are difficult to measure in economic terms using standard methods, some difficult-to-quantify harms from the analysis are excluded from the analysis. The estimates presented here are therefore conservative.

17. The next three sections of my Report correspond to the three parts of my assignment. In Section II, I discuss the economic analysis of a public nuisance. In Section III, I identify and quantify in economic terms the net costs in the Cabell Huntington Community due to the sales and distribution of prescription opioids. I cover costs in six groups of harms: mortality, morbidity from opioid-use disorder, neonatal abstinence syndrome, crime, loss of residential property value, and child maltreatment. Within the discussion of morbidity, I consider potentially offsetting economic benefits of prescription opioids in terms of workforce participation. Section IV summarizes the cost analysis and concludes that these costs are of sufficient magnitude to regard the sales and distribution of prescription opioids as constituting a public nuisance in the Cabell Huntington Community.

II. The Economic Analysis of Public Nuisances

18. I rely on the long tradition within the field of economics analyzing the social consequences of private behaviors imposing costs on others. A public nuisance occurs when an action (or set of actions) undertaken by a party (or group of parties) gives rise to overwhelming "negative externalities." An externality "occurs whenever the actions of one party make another

party worse or better off, yet the first party neither bears the costs nor receives the benefits of doing so."[15]

19. A negative externality imposes costs on others. An example of a negative externality is pollution of a river.[16] If a household or firm deposits waste in the river, other members of the community are harmed (*e.g.*, bear health risks, enjoy less recreational use of the river) but they are not compensated for the costs imposed on them. In economics, harms, such as health risks or loss of recreational opportunities, are regarded as a "cost" imposed on others and can be valued in dollar terms.

20. The legal concept of a public nuisance parallels the concept of a negative externality in economics, as has been recognized in legal scholarship: "Nuisance may also be viewed as a form of externality that interferes with the enjoyment or use of another's property."[17]

21. In a related approach, scholarship in law and economics sometimes refers to a public nuisance as a "public bad:" "The common law of public nuisance has evolved for dealing with public bads. When an agent imposes a cost, similar in amount and kind, on a group of individuals, then the harmed group can call upon a public defender to bring a public nuisance action against the agent."[18] "Public bads are ... said to emerge when a large number of parties are affected negatively and simultaneously, at the margin, by an action undertaken by an individual or group. The nature of the phenomenon is such that there is no low-cost way to insulate and partition the affected individuals in the group from the negative effect. What one group member receives, all receive."[19] I will use the economic concepts of public bad and

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[15] J. Gruber, *Public Finance and Public Policy*, 5th edition, 2016, p. 124.

[16] An externality can be positive as well, that is, confer benefits on others. A neighborhood association might maintain a local park that is open to the public, benefiting those outside the immediate neighborhood as well as residents of the neighborhood.

[17] T. Swanson and A. Kontoleon, "Nuisance (Section 2100)," in B. Bouckaert and G. de Geest (eds.), *Encyclopedia of Law and Economics*, 2000, pp. 380-402 at 382. See also, R. Cooter and T.S. Ulen, *Law and Economics*, 6th Edition, Berkeley Law Books, 2016, p. 168, and K. Hylton, *op. cit*.

[18] K. Boudreaux and B. Yandle, "Public Bads and Public Nuisance-Common Law Remedies for Environmental Decline," *Fordham Environmental Law Review*, 14(1), Article 2, 2002, pp. 55-88 at p. 65.

[19] *Ibid.*, pp. 59-60.

negative externality in determining whether the sales and distribution of prescription opioid products constitute a public nuisance to the Cabell Huntington Community in economic terms.[20]

III. Economic Costs Imposed by the Sales and Distribution of Prescription Opioid Products in the Cabell Huntington Community

22. I quantify the net economic costs relating to deaths, morbidity, neonatal abstinence syndrome, crimes, property value loss, and child maltreatment in the Cabell Huntington Community over the period 2006 to 2018, unless otherwise noted. The methods I use to estimate costs of the components listed above are consistent with similar analyses conducted by numerous public and private agencies throughout the United States.[21]

23. It is difficult to overstate the impact of the opioid epidemic on the Cabell Huntington Community. West Virginia, and Cabell County in particular, is near the top of the nation on opioid overdose rates (fatal and non-fatal), number of babies born with neonatal abstinence syndrome (NAS), and the number of prescription opioids dispensed (both in absolute number and per capita). The opioid epidemic has contributed to outbreaks of other diseases, such as Hepatitis C and HIV, and led to burnout and trauma amongst police officers, fire fighters, emergency medical technicians, and other first responders. The unprecedented numbers of

[20] The relationship between public bad and negative externality is the same as between public good and positive externality. A public good involves positive externalities, but not all externalities are public goods. Pure public goods must be consumed in equal quantity by all and are completely non-rivalrous, *i.e.*, the consumption by one person does not affect the consumption by others. The classic papers are: P.A. Samuelson, "The Pure Theory of Public Expenditure," *Review of Economics and Statistics,* 36(4), 1954, pp. 387-389, and P.A. Samuelson, "Diagrammatic Exposition of a Theory of Public Expenditure," *Review of Economics and Statistics,* 37(4),1955, pp. 350-356. Not all externalities possess these two characteristics in pure form, so I use the more general term, "externality."

[21] National studies include The Council of Economic Advisers (CEA), Executive Office of the President of the United States, "The Underestimated Cost of the Opioid Crisis," November 2017 (https://www.whitehouse.gov/sites/whitehouse.gov/files/images/The%20Underestimated%20Cost%20of%20the%20Opioid%20Crisis.pdf); C.S. Florence, *et al.*, "The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013," *Medical Care*, 54(10), 2016, pp. 901-906; C. Rhyan, "The Potential Societal Benefit of Eliminating Opioid Overdoses, Deaths, and Substance Use Disorders Exceeds $95 Billion Per Year," *Altarum*, November 16, 2017; and S. Davenport, A. Weaver and M. Caverly, "Economic Impact of Non-Medical Opioid Use in the United States: Annual Estimates and Projections for 2015 through 2019," Society of Actuaries, 2019. The CEA studies costs of illicit and prescription opioids; Florence and coauthors work at the Center for Disease Control (CDC) and study costs of prescription opioid products; Rhyan studies costs of prescription and illicit products; and Davenport and his coauthors also study costs of prescription and illicit products.

babies born with NAS will have long-lasting effects. The ravages of the opioid epidemic are far-reaching, affecting virtually all residents in the Community, much of it documented via media coverage on the different facets of the epidemic.[22] The opioid epidemic has increased criminal activity, reduced housing values, and imposed a general loss of well-being in this Community.

24. Few communities have been hit as hard by the opioid epidemic as has the Cabell Huntington Community. A recent American Enterprise Institute (AEI) report analyzed the geographic variation of per capita costs due to the opioid crisis by state and county. The report identifies West Virginia as incurring the highest cost per capita among all states and Cabell County as ranking number 3 among over 3,000 counties nationwide.[23]

25. The local response to the crisis has been equally forceful. Cabell Huntington Community leaders, policy makers, and public servants have launched a multipronged effort to study and combat the opioid epidemic. The Huntington Mayor's Office released comprehensive plans aimed at fighting the opioid epidemic focused on bolstering prevention efforts, providing greater access to a broader set of treatment services, and mitigating the inflow of opioids via law enforcement initiatives.[24] Huntington's Marshall University published the *Resiliency Plan*, a comprehensive guide for responding not only to the short-term issues associated with the opioid epidemic, but also preparing for its long-term economic and legal consequences.[25] The City of

[22] Examples of national coverage of the Cabell Huntington Community's opioids epidemic include the Netflix Documentary "Heroin(e)" (https://recoveryboysthefilm.com/about-heroine/); a STAT profile: A. Joseph, "26 Overdoses in Just Hours: Inside a Community on the Front Lines of the Opioid Epidemic," *STAT*, August 22, 2016; and multimedia coverage by *The Atlantic*, entitled "A Heroin Hearse in the OD Capital of America" (https://www.theatlantic.com/video/index/586753/heroin-hearse/).

[23] See Tables 1 and 2 in A. Brill and S. Ganz, "The Geographic Variation in the Cost of the Opioid Crisis," American Enterprise Institute (AEI), Working Paper 2018-03, March 2018. They "estimate per-capita state-level and county-level non-mortality and total economic burdens of the opioid crisis in 2015 by distributing national estimates based on variation in local wages, health care costs, and criminal justice costs along with variation in opioid-related death and addiction rates, and average age-adjusted value of statistical lives lost.".

[24] City of Huntington, Mayor's Office on Drug Control Policy, "2015 Strategic Plan," August 24, 2015 and then approximately two years later the "Two-Year Strategic Plan for Addressing the Opioid Crisis in the City of Huntington/Cabell and Wayne Counties, West Virginia" was released, May 2017.

[25] "Resiliency Plan Cabell County, WV," Division of Addiction Sciences, Marshall University Joan C. Edwards School of Medicine, January 2020 (https://jcesom.marshall.edu/media/58477/2020_cabell-county-resiliency-plan_final.pdf).

Huntington compiled its successes (and failures) in *The City of Solutions*, providing guidance to other communities facing the opioid epidemic.[26]

26. These reports depict the myriad ways prescription opioids imposed harms in the Community.[27] For example, the Mayor's "2015 Strategic Plan" notes, among other harms, that babies born with NAS cost significantly more than babies born without NAS: the later cost around $10,000, whereas NAS births can be as much as $55,000.[28] In another example, a review conducted by Marshall University found that state and local entities devote significant financial resources to opioid epidemic harm-reduction programs, including distribution of naloxone to local emergency units (*e.g.*, in 2016, the administration of 4,186 doses of the opioid antagonist).[29]

27. The Cabell Huntington community has taken concrete actions to deal with harms. Treatment centers such as Lily's Place, Project Hope, and Healthy Connections, as well as the establishment of the Drug Court, focused on rehabilitation over punishment, are designed to aid those currently fighting drug addiction. These initiatives have required outsized efforts and resources.[30]

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[26] "The City of Solutions, Huntington WV: A Guide to What Works (and What Does Not) in Reducing the Impact of Substance Use on Local Communities," edited by J. Maiolo, Division of Addiction Sciences in the Department of Family and Community Health at the Marshall University Joan C. Edwards School of Medicine, September 2019 (philanthropywv.org/content/uploads/2019/11/COS-Guidebook-Finalized-as-of-9-26-19.pdf), hereafter, The City of Solutions, Huntington, WV.

[27] In 2015, Fire Chief Jan Rader compiled an annual estimate of medical costs of drug abuse in Cabell County. This estimate was introduced as a series of exhibits in Mr. Lemley's deposition (See Deposition of Scott Lemley, in this matter, July 3, 2020 (hereafter, Lemley Deposition), Exhibits 32-35). She identified average costs for the following categories related to drug abuse: overdose calls, overdose calls with hospitalization, drug use complications related to cellulitis, endocarditis, and osteomyelitis, NAS, hepatitis B and C without a transplant and liver transplant. Her total estimated cost was $30.5 million. This compilation of costs illustrates some aspects of the costs resulting from the opioid epidemic.

[28] City of Huntington, "2015 Strategic Plan," *op. cit.*, p. 11.

[29] N. Bowden, *et al.*, "The Cost of the Opioid Epidemic in West Virginia," presented at the 54th Annual MBAA Conference, Chicago, IL, April 2018. While the initial expenses were paid by a federal grant, the growing need for opioid antagonists prompted the state of West Virginia to purchase 34,000 doses in 2018 at a cost of approximately $1,000,000. See West Virginia Department of Health and Human Resources, "DHHR Begins Distributing Naloxone Statewide for First Responders," June 5, 2018 (https://dhhr.wv.gov/News/2018/Pages/DHHR-Begins-Distributing-Naloxone-Statewide-for-First-Responders---.aspx).

[30] Some examples of these costs are available in The City of Solutions, Huntington WV, pp. 63-66.

28. Deposition testimony by county and city personnel confirm the profound impact of the opioid epidemic on the Cabell Huntington Community:

- Raymond Canafax, Deputy Chief of the Huntington Fire Department, testified: "But this – in my experience, this – this didn't know any bounds, this epidemic. It was in all neighborhoods. It was in the best of neighborhoods and the worst of neighborhoods and the best – the best of homes to the worst of homes."[31]
- Jan Rader, Fire Chief for the City of Huntington, testified: "There's not one person in this area that I know that has not been touched or had collateral damage to them, themselves from the … opioid epidemic. It is horrendous."[32]
- Sue Ann Painter, the executive director of the board of registered nurses, testified: "It's been financially devastating to people with substance use disorder and their families and their communities. It has emotional impact on all the individuals involved, and people die of overdose."[33]
- Craig Preece, a long-time Huntington Police Department officer, testified: "…looking back over those 22 years, that opioids and everything that came after prescription meds, that's what was the most damaging … to the City as far as people and maybe their quality of life. "[34]
- Officer Preece adds, describing to the impact opioids have had on the City of Huntington that: "It's resulted in a lot of deaths. It's resulted in a lot of criminal charges. It's resulted in people that remain addicted that continue to seek opioid type drugs to this day. There's been robberies, thefts and violence associated with the drug."[35]

29. While I quantify some of the harms identified above, my valuations omit aspects of the harms that are difficult to measure with standard economic methods or for which data are unavailable as a basis for reliable estimates. For example, babies born with NAS incur higher health care expenditures at birth, which I am able to quantify. However, there is also evidence that these babies are more likely to suffer a range of health consequences later in life and to have poor economic outcomes, but due to data limitations, I am unable to fully quantify these aspects of the harms. Similarly, the stress from increasing numbers of overdoses has very real psychological consequences for first responders, which ultimately affects recruitment and

[31] Deposition of Raymond Carafax, in this matter, June 16, 2020 (hereafter, Carafax Deposition), p. 120.

[32] Deposition of Jan Rader, in this matter, June 17, 2020 (hereafter, Rader Deposition), pp. 78-9.

[33] Deposition of Sue Ann Painter, in this matter, June 26, 2020, p. 162.

[34] Deposition of Craig Preece, in this matter, July 14th, 2020 (hereafter, Preece Deposition), p. 298.

[35] Preece Deposition, pp. 298-99.

retention of these critical public servants. Here again, due to data limitations, I am unable to fully quantify these harms resulting from the sales and distribution of prescription opioids. Moreover, while the opioid crisis harms the Cabell Huntington Community, due to data limitations, most of my harm qualifications are limited to Cabell County.[36]

30. The sales and distribution of massive volumes of prescription opioids into the Community has had devasting downstream consequences. One of the central facts of the opioid epidemic is that the majority of individuals who misuse opioids began with prescription opioids before turning to heroin, or other opioids.[37] For example, Cerda, *et al.* (2015) find that among children and adolescents, prior non-medical use of prescription opioids was strongly predictive of later use of heroin.[38] Non-medical use of prescription opioids is defined as "…both using prescription opioids more often or longer than prescribed, or use of prescription opioids without a prescription."[39]

31. Dr. Lembke in her report, explains that the "gateway effect" of prescription opioids includes the transition from medical use of prescription opioids to non-medical use.[40] Among other studies, Dr. Lembke cites McCabe, *et al.*, in the journal *Pediatrics*, in which the "gateway

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[36] Except for crime, where I use data for the entire city from the City of Huntington Police Department, my harm valuations exclude the portion of Huntington located in Wayne county.

[37] There is substantial evidence that the gateway to illicit opioids is prescription opioids. For examples, see C.M. Jones, "Heroin Use and Heroin Use Risk Behaviors Among Nonmedical Users Of Prescription Opioid Pain Relievers – United States, 2002-2004 And 2008-2010," *Drug and Alcohol Dependence*,132, 2013, pp. 95-100 (found that between the periods of 2002-2004 and 2008-2010, there was an increase of heroin use among people who had used opioid pain relievers non-medically in the past year); P.K. Muhuri, J.C. Gfroerer, and M.C. Davies, "Associations of Nonmedical Pain Reliever Use and Initiation Of Heroin Use in The United States," CBHSQ Data Review, August 2013 (showed that the incidence of heroin use (from 2002-2011) was 19 times higher among those reporting prior non-medical pain reliever use, compared to those who had not used pain relievers non-medically); T.J. Cicero, M.S. Ellis, H.L. Surratt, and S.P. Kurtz, "The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years," *JAMA Psychiatry*, 71(7), 2014, pp. 821-826 (found, among other things, that 75% of patients seeking treatment for heroin abuse from 2004-2014 had been introduced to opioids through prescription drugs); and G. Banerjee, *et al.*, "Non-medical Use of Prescription Opioids is Associated with Heroin Initiation Among US veterans: a Prospective Cohort Study," *Addiction*, 111, 2016, pp. 2021-2031 (estimated the influence of non-medical use of prescription opioids on heroin initiation in U.S. veterans receiving medical care and found that non-medical use of prescription opioids was associated positively and independently with heroin initiation).

[38] M. Cerda, *et al.*, "Nonmedical Prescription Opioid Use in Childhood and Early Adolescence Predicts Transitions to Heroin Use in Young Adulthood: A National Study," *Journal of Pediatrics*, 167(3), September 2015, pp. 605-12. See also, Cicero, *et al*., *op. cit.*

[39] Expert Report of Professor Katherine Keyes, in this matter, August 3, 2020 (hereafter Keyes Report), p. 7.

[40] Expert Report, Anna Lembke, M.D., in this matter, August 3, 2020 (hereafter Lembke Report), Paragraph C.8.

effect" refers to the transition from medical to non-medical use of prescription opioids, and subsequent use of illicit opioids.[41] The massive inflow of prescription opioids into the Cabell Huntington Community permitted diversion to non-medical use of prescription opioids.[42] Numerous studies find that most non-medical users obtain opioids at some point from a medical provider and/or from family/friends who obtained them from a medical provider.[43] Moreover, Dr. Smith, an epidemiologist and professor at West Virginia University, Department of Epidemiology, notes that the overdose data he analyzes "support the recognized transition from prescription to illicit opioids use, which has been documented in numerous peer-reviewed studies of the US population in general, and…the same thing occurred throughout West Virginia, including Cabell County."[44]

32. Deposition testimony confirms that prescription opioids are a gateway to other opioids in the Community:

- Jan Rader, Fire Chief, testified: "When people who were addicted couldn't find the pills that they had been on for years, they turned to heroin because it was cheaper and easier to obtain. They were using a needle to invite it into their body, spreading bacteria. You had all kinds of medical complications associated with it. But again, probably 80 percent of them - especially in my experience - started with a legal prescription."[45]

- Paul Hunter, a Huntington Police Sergeant and part of the Drug ad Violent Crimes Task Force as well as head of the City Law Enforcement Narcotics Unit, testified: "The heroin appeared to come into existence, or the use of it, shortly after prescription pills were a problem. And just from my investigation, talking to cheaper version and it was easier to get at times. They started getting heroin."[46]

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[41] S.E. McCabe, *et al.*, "Trends in Medical and Nonmedical use of Prescription Opioids Among US Adolescents: 1976–2015," *Pediatrics*, 139(4), 2017, pp. 1-9. The Lembke Report discussion of the McCabe, *et al.* study is on paragraph C.8.d, p. 132

[42] Keyes Report, Opinion 5, p. 5.

[43] R.N. Lipari and A. Hughes, "How People Obtain the Prescription Pain Relievers they Misuse," The CBHSQ Report: January 12, 2017, Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Rockville, MD; J.A. Inciardi, H.L. Surratt, T.J. Cicero, S.P. Kurtz, S.S. Martin, and M.W. Parrino, "The 'Black Box' of Prescription Drug Diversion," *Journal of Addictive Diseases*, 28(4), 2009, pp. 332-347.

[44] Expert Report, Gordon Smith, M.D., in this matter, August 3, 2020 (hereafter Smith Report), p. 10.

[45] Rader Deposition, pp. 85-86.

[46] Deposition of Paul Hunter, in this matter, July 1, 2020, p. 246.

33. From an economic standpoint, the costs due to the sales and distribution of prescription opioids include costs for which prescription opioids are the proximate cause (*e.g.*, a death from overdose of prescription opioids) and those for which prescription opioids were the ultimate but not necessarily the proximate cause (*e.g.*, a death from fentanyl for someone using fentanyl because of their start on prescription opioids). Dr. Lembke, a physician,[47] and Professor Keyes, an epidemiologist,[48] elaborate on the role of prescription opioids as a gateway drug.

A. Mortality

Overview

34. The economic cost of mortality attributed to the sales and distribution of prescription opioid products is the number of deaths due to these sales and distributions in the Cabell Huntington Community multiplied by the value of each life lost.

35. The valuation undertaken in this section is conservative in that it values a life only in terms of the "willingness to pay" of the person at risk of death. Beyond the self-evident harm of the loss of life to the victim, an opioid-overdose death impacts families and the Cabell Huntington Community in ways difficult to value with economic methods. For example, in 2018, about 55% of West Virginia's opioid fatalities were adults between 25-44,[49] many of whom were parents caring for small children.[50] Harms to these children go unmeasured in my valuation of a death. A death is a loss of companionship and friendship to spouses or romantic partners, friends, and the community. These harms go unmeasured in my valuation. Moreover, Cabell Huntington Community first responders face increased job stress due to ongoing dealings with large numbers of fatal opioid overdose fatalities. This increased stress on first responders

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[47] Lembke Report, Paragraph C.8.g, p.134.

[48] Keyes Report, p. 44 contains a discussion of the causal link between prescription opioids and subsequent heroin use.

[49] Kaiser Family Foundation analysis of Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. Multiple Cause of Death 1999-2018 on CDC WONDER Online Database, released 2020. Data are from the Multiple Cause of Death Files, 1999-2018, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed on February 13, 2020. The calculation is the ratio of the deaths for people aged 25-44 (387) and the total number of deaths (702). See http://www.kff.org/other/state-indicator/opioid-overdose-deaths-by-age-group.

[50] C. Levine, *et al.*, "The Statistics Can't Capture the Opioid Epidemic's Impact on Children." *STAT*, December 30, 2017 (www.statnews.com/2018/01/02/opioid-epidemic-impact-children/).

results in public sector costs for training and counseling for firefighters, police officers and EMS personnel,[51] results in what has been called "compassion fatigue"[52] that takes a personal toll,[53] and results in difficulties retaining personnel.[54] Deputy Chief Canafax commented on compassion fatigue: "Our firefighters were getting exhausted, and were – both mentally and physically, and this was affecting their mental wellbeing."[55] These human and economic tolls on first responders are also not quantified in my valuation of a death attributed to prescription opioids.

36. While the opioid epidemic has taken an enormous toll in the United States, the Cabell Huntington Community has been especially hard hit. Figure 2 depicts the outsized harm suffered by Cabell County in the form of prescription opioid-related deaths. The data come from Professor Keyes' report, and compare the rate of deaths proximately caused by prescription opioids in Cabell County, West Virginia and the United States from 1999-2018.[56] West Virginia was hit harder than other states, and within West Virginia, Cabell was hit harder than other counties.

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[51] The City of Solutions, Huntington WV, p. 54.; "Resiliency Plan for Cabell County," *Division of Addiction Sciences*, Marshall University Joan C. Edwards School of Medicine, January 2020 (https://jcesom.marshall.edu/media/58477/2020_cabell-county-resiliency-plan_final.pdf/).

[52] See E.L. Winstanley, "The Bell Tolls for Thee & Thine: Compassion Fatigue & the Overdose Epidemic," *International Journal of Drug Policy*, June 1, 2020.

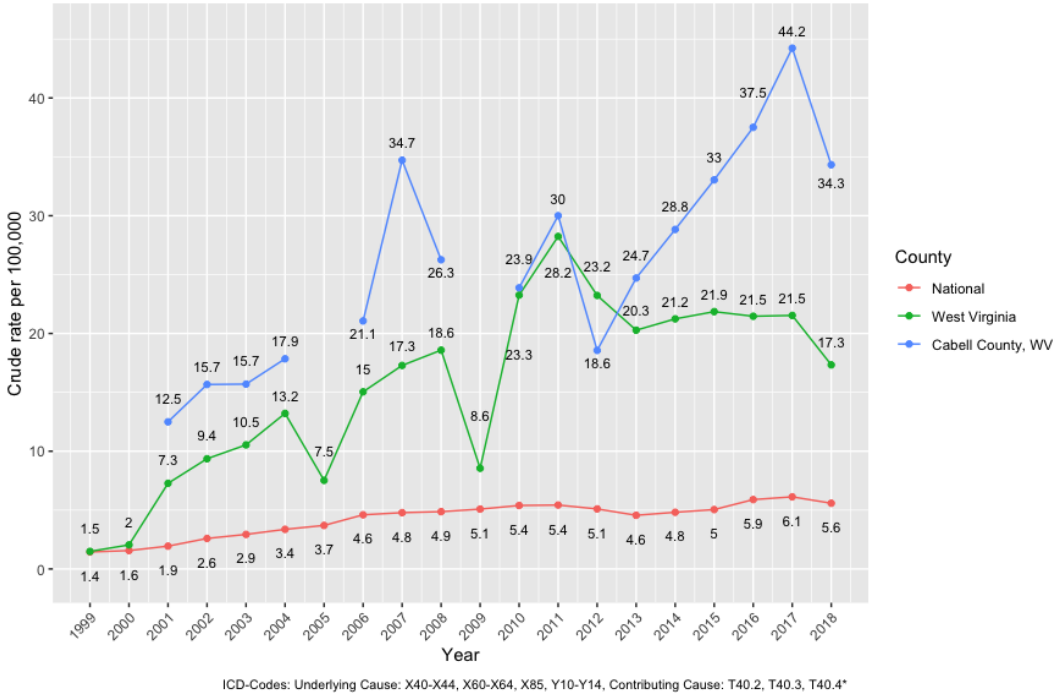
[53] The City of Solutions, Huntington WV, p. 42.

[54] See interview with Fire Chief Jan Rader, Medium.com/@BloombergCities, "How One Fire Chief is Fighting 'Compassion Fatigue' as Overdoses Mount," May 10, 2018 (https://medium.com/@BloombergCities/how-one-fire-chief-is-fighting-compassion-fatigue-as-overdoses-mount-f4c193323922).

[55] Canafax Deposition, p. 118.

[56] Keyes Report, Figure 8. See page 31 of her report for a description of the methodology and sources for these figures.

Figure 2
Prescription Opioid Death Rates
National, West Virginia and Cabell County Rates
Replication of Keyes Report, Figure 8



Count of Deaths

37. Professor Keyes identifies the number of deaths due to the sales and distribution of prescription opioids for Cabell County residents in each year from 2006 to 2018.[57] My Table 2 takes the numbers from Figure 16 from the Keyes Report. Professor Keyes explains her estimates of the number of deaths due directly and indirectly to prescription opioids:

> "Opioid overdose deaths for which a prescription opioid was listed on the death certificate as a contributing cause are deemed directly due to prescription opioids. Among other deaths, I estimate that a minimum of 53.4% of deaths are indirectly due to prescription opioids, given the NSDUH data estimates of the proportion of non-prescription opioid use disorder for which prescription opioids were a preceding substance use. Therefore, Figure 16 provides the total number of opioid overdose deaths

[57] Keyes Report, Figure 16.

in Cabell County for each year from 2006 through 2018, with the number directly attributable and minimum number indirectly attributable to prescription opioids."[58]

38. I rely on Professor Keyes' estimates of deaths due to prescription opioids for my mortality counts.

39. Deaths in Cabell County due to all opioids went up by a factor of four or more between the early and more recent years in the data. Over the entire time period, over half of deaths, approximately 85.4% (556/651) were due directly to prescription opioids. 52 deaths were from a non-prescription opioid that were attributable to the user starting on prescription opioids. Deaths in this category in Cabell County spiked in the 2015-2018 period.

Table 2
Deaths Due to Prescription Opioids in Cabell County
2006-2018

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
All deaths due to opioids	21	37	25	5	25	36	22	42	45	69	87	132	105	**651**
Deaths directly due to prescription opioids	20	33	25	5	23	29	18	26	32	48	69	124	104	**556**
Deaths due to non-prescription opioids	1	4	0	0	2	7	4	16	13	21	18	8	1	**95**
Deaths due to non-prescription opioids due to prescription opioids	1	2	0	0	1	4	2	9	7	11	10	4	1	**52**
Total deaths due to prescription opioids	**21**	**35**	**25**	**5**	**24**	**33**	**20**	**35**	**39**	**59**	**79**	**128**	**105**	**608**

Sources: Keyes Report, Figure 16.

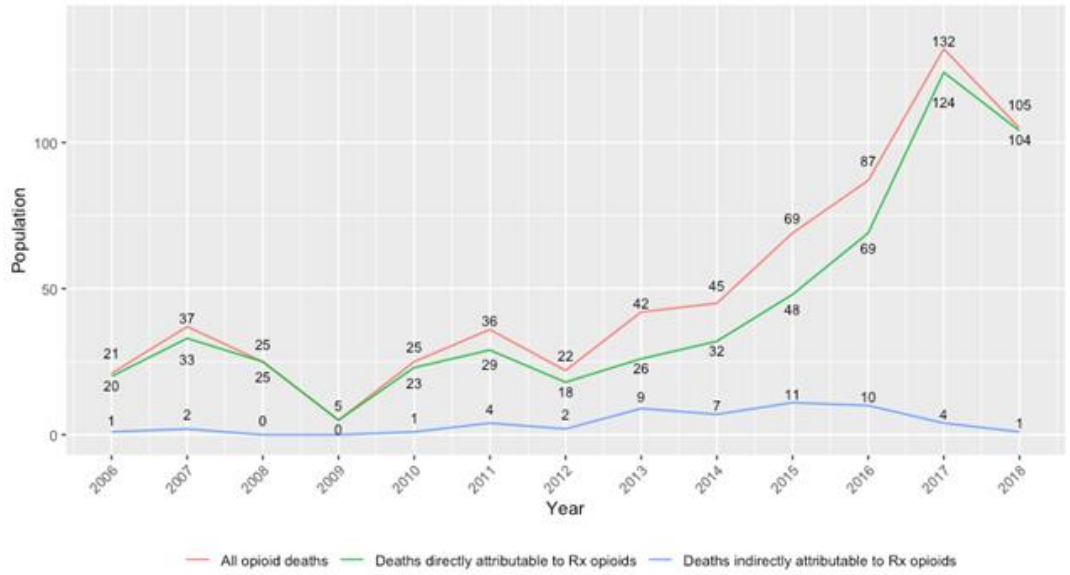
40. In total, over the period 2006-2018, 608 Cabell County residents died due to the sales and distribution of prescription opioids. The economic cost of these deaths constitutes the largest component of the harms assessed in this Report, consistent with the findings of other studies of the costs of the opioid epidemic.[59]

[58] Keyes Report, p. 48.

[59] For example, the CEA's "The Underestimated Cost of the Opioid Crisis," *op. cit.*, finds that costs associated with mortality, using a similar approach to value attribution that I use in this Report, based on the Value of a Statistical Life (VSL) account for about 84% of the total of mortality and morbidity costs. The CEA report refers to these as "fatality" and "non-fatality" costs. See CEA (2017), Table 2. The 84% is based on the "middle" estimate of the VSL contained in the table.

41. Figure 3 graphs the data from Table 2, displaying the massive growth in deaths due to prescription opioids over the period 2006 to 2018. The figure conveys visually that the vast majority of the deaths were directly due to prescription opioids.

Figure 3
Deaths Due to Prescription Opioids in Cabell County
2006-2018
Replication of Keyes Report, Figure 16



Valuation of Deaths

42. An accounting of the economic cost of a death can be made with the economic concept of the value of a "statistical life," used by researchers and government agencies to assign a dollar value to the economic cost of a death.[60] I rely on guidance from the Assistant Secretary for Planning and Evaluation (ASPE) of the U.S. Department of Health and Human Services (HHS)

[60] The VSL is figured as the ratio of the maximum willingness to pay for a given reduction in the probability risk of death within a specified time period. This yields a monetary amount per statistical life saved. For example, if I were willing to pay $10,000 to avoid a 1/100 risk of death, the VSL would be measured as $10,000*100 = $10m. See L. Robinson and J. Hammitt, "Valuing Reductions in Fatal Illness Risks: Implications of Recent Research," *Health Economics*, 25, 2016, pp 1039-1052. The methodology for measuring the VSL is discussed in more detail in Appendix C.

and use $9.3 million as the national value of a statistical life (VSL) in 2014.[61] The national value of $9.3 million in 2014 can be adjusted using standard methods to different years and different geographic areas; I refer to this as the adjusted VSL. Price levels are adjusted based on the annual values of the Consumer Price Index (CPI). My VSL estimate is also adjusted for the differences in income between the national estimate and Cabell County for each year.

43. Table 3 takes the total number of deaths attributed to the sales and distribution of prescription opioids in Cabell County from 2006-2018 from Table 2, and multiplies each death by the adjusted VSL for each year for Cabell County.[62] Over this 13-year time period, the measure of the economic value of lost lives is over $3.43 billion for Cabell County.[63]

Table 3
Valuation of Mortality Due to Prescription Opioids in Cabell County
2006-2018

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
Total deaths attributed to prescription opioids	21	35	25	5	24	33	20	35	39	59	79	128	105	608
VSL ($millions)	$4.6	$3.9	$4.2	$4.8	$5.2	$5.7	$5.4	$6.3	$5.1	$6.3	$6.4	$5.2	$6.5	
Valuation ($millions)	$96.1	$137.5	$104.6	$24.0	$125.5	$186.6	$107.2	$219.1	$200.5	$373.3	$505.9	$671.2	$686.2	$3,437.8

Sources: Appendix C, Section I.

B. Morbidity

Overview

44. The sales and distribution of prescription opioids contribute to opioid-related morbidity. Morbidity simply means to have a disease or be in ill health. The economic valuation in this

[61] Office of the Assistant Secretary for Planning and Evaluation (ASPE), U.S. Department of Health and Human Services (HHS), "Guidelines for Regulatory Impact Analysis," 2016 (https://aspe.hhs.gov/system /files/pdf/242926/HHS_RIAGuidance.pdf) (hereafter, "HHS 2016 Guidelines").

[62] See Appendix C for a description of the adjustments made.

[63] The HHS Guidelines report lower and upper bounds for national VSL of $4.4 million and $14.2 million for 2014. Using these values instead of the average used above results in an economic value of lost lives of $1.6 billion and $5.3 billion, respectively. Note that the number of intentional deaths data in Cabell County are too few to determine a reliable estimate. Data are suppressed due to small numbers in several years during this period. I therefore make no adjustments for intentional deaths in this report. See Keyes Report, p. 33.

section is the number of cases of Opioid Use Disorder (OUD) due to prescription opioids multiplied by the excess health care costs associated with the treatment of OUD and *sequelae*.

45. OUD is a substance use disorder characterized by impaired control over opioids use, including but not limited to the need to use more opioids to achieve desired effects, withdrawal symptoms upon cessation of use, and adverse social, interpersonal, occupational, and physical consequences of opioid use.[64] The diagnosis of OUD is used by health care providers and criteria are included in major disease classification systems such as the Diagnostic and Statistical Manual of Mental Health Disorders (DSM).[65] According to the federal Centers for Disease Control and Prevention (CDC), based on household surveys, there were at least 2.1 million Americans with OUD as of 2017.[66]

46. As is the case with mortality, OUD morbidity has hit the Cabell Huntington Community harder than other parts of West Virginia, and by an even larger margin, other parts of the country as a whole. Figure 5 shows the prevalence of OUD in Cabell County, West Virginia, and the United States from 2006-2018.[67]

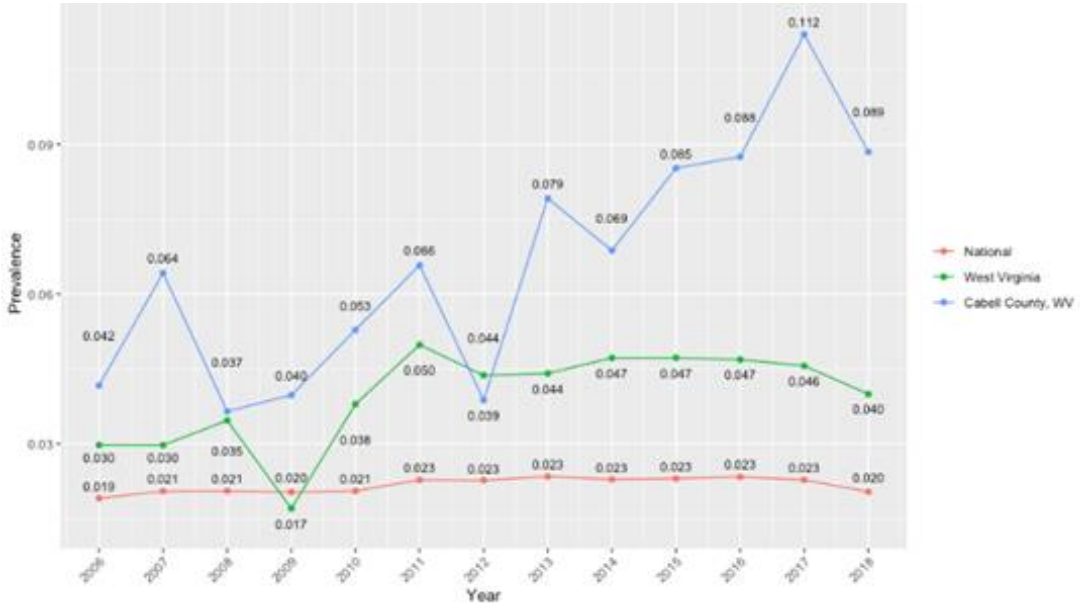
[64] See Keyes Report, Section III, pp. 7-8 for a discussion on the distinction between OUD, opioid abuse, and opioid dependence, which are defined *disorders*. Professor Keyes also discusses related *symptoms*, such as physical opioid dependence, opioid tolerance, and withdrawal which are included in the definition of OUD.

[65] *Ibid.*

[66] CDC and U.S. Department of Health and Human Services, "Annual Surveillance Report of Drug-Related Risks and Outcomes – United States, Surveillance Special Report," 2019 at p. 17.

[67] Keyes Report, Figure 13.

Figure 5
OUD Prevalence
National, West Virginia and Cabell County
Replication of Keyes Report, Figure 13



Count of Morbidity

47. Table 4 takes numbers from Keyes Report Figure 14 for the estimated number of residents of Cabell County with OUD and those with OUD attributable to prescription opioids over the years 2006-2018.[68] The first row of the Table reports the number of all cases of OUD. The second row contains the number of cases of OUD Professor Keyes attributes directly due to prescription opioids.[69] Among the cases of OUD not directly due to prescription opioids (third row of Table 4), Professor Keyes attributes a share of these indirectly to prescription opioids. Professor Keyes' estimates of the number of cases of OUD due to non-prescription opioids that are ultimately due to prescription opioids are in the fourth row of the Table. Specifically, Professor Keyes opines that "…a minimum of 53.4% of opioid use disorder cases and deaths in the Cabell Huntington Community are indirectly attributable to prescription opioids, averaged

[68] Keyes Report, Figure 14 (p. 42).

[69] Keyes Report, Figure 14 (p. 42).

across years from 2006 to 2014."[70] The total number of people with OUD in each year in Cabell County attributable to prescription opioids (fifth row) is the sum of those with OUD due to prescription opioids, and those with OUD from other opioids that is attributable to opioid prescriptions.[71] In terms of a share, as shown in the sixth row, Professor Keyes' estimates imply that from 2006 – 2018, over 90% of OUD cases in Cabell County are ultimately due to prescription opioids.

Table 4
Morbidity Due to Prescription Opioids in Cabell County
2006-2018

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
All OUD cases	3,959	6,105	3,475	3,819	5,089	6,359	3,763	7,692	6,677	8,257	8,403	10,643	8,252	82,493
OUD cases directly due to prescription opioids	3,745	5,776	3,385	3,721	4,867	6,083	3,264	6,674	5,267	6,076	5,711	7,156	5,800	67,525
OUD cases due to non-prescription opioids	214	329	90	98	222	276	499	1,018	1,410	2,181	2,692	3,487	2,452	14,968
OUD cases due to non-prescription opioids due to prescription opioids	114	176	48	52	118	147	266	544	753	1,164	1,437	1,862	1,309	7,990
Total OUD cases due to prescription opioids	**3,859**	**5,952**	**3,433**	**3,773**	**4,985**	**6,230**	**3,530**	**7,218**	**6,020**	**7,240**	**7,148**	**9,018**	**7,109**	**75,515**
Share of OUD cases due to prescription opioids	97.5%	97.5%	98.8%	98.8%	98.0%	98.0%	93.8%	93.8%	90.2%	87.7%	85.1%	84.7%	86.1%	91.5%

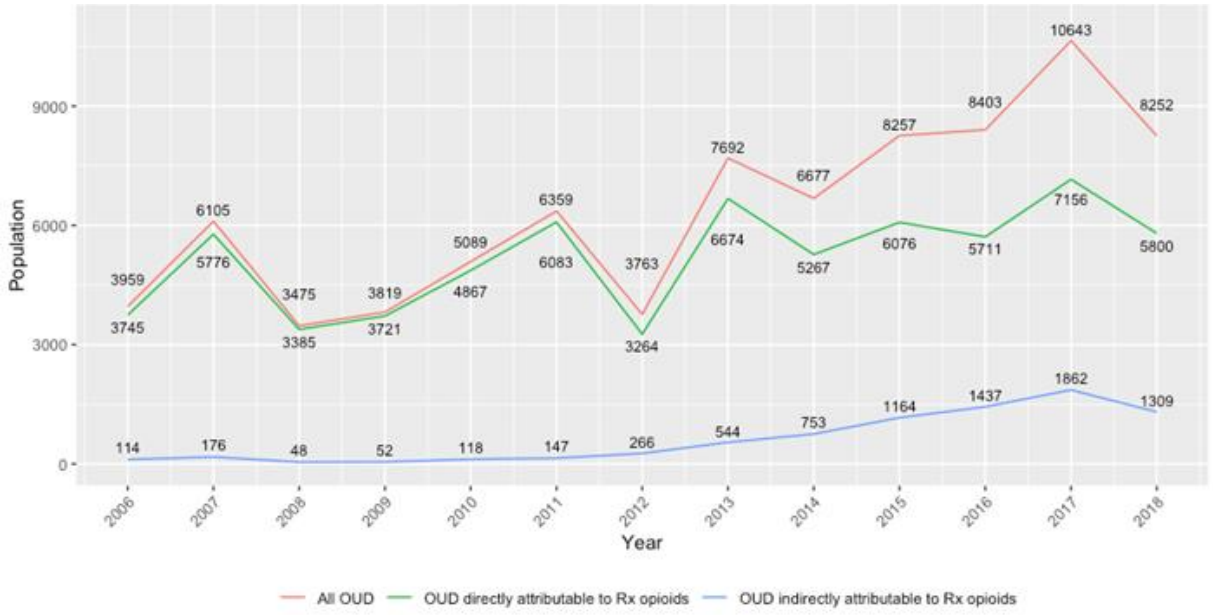
Sources: Keyes Report, Figure 14.

48. Figure 6 graphs the data from Table 4, depicting the rise in the number of OUD cases. In the later years, cases of OUD due to non-prescription opioids attributable to prescription opioids make up a larger share of the total.

[70] Keyes Report, p. 48.

[71] See Keyes Report, pp. 47-48, for a description of the methodology used to compile these estimates.

Figure 6
Morbidity Due to Prescription Opioids in Cabell County
2006-2018
Replication of Keyes Report, Figure 14



Valuation of Morbidity

49. I conservatively value the economic effects of morbidity attributed to opioid prescriptions in terms of higher health care costs. The opioid epidemic has increased health care utilization. Individuals with OUD consume more health care both to treat their OUD (*e.g.*, addiction services, MOUD, etc.) and to treat comorbidities, such as hepatitis C and HIV, which occur in greater frequencies among patients with OUD.[72] Researchers examining the additional health care costs resulting from OUD have measured the magnitude of excess health care costs due to OUD applying a "cost-of-illness" methodology. The basic approach compares the health care costs of individuals with OUD to a comparison group of individuals with similar insurance, sociodemographic, and other characteristics. The goal is to compare the costs for all health care,

[72] J.S. Morrison and L. Dattilo, "America's Dangerous Syndemic: Opioid Addiction, HIV, and Hepatitis C," *Center for Strategic & International Studies*, December 2017; P.J. Peters, *et al.*, "HIV Infection Linked to Injection Use of Oxymorphone in Indiana, 2014-2015," *New England Journal of Medicine*, 375(3), 2016, pp. 229-239; E. Nilsen, "America's Opioid Crisis has Become an 'Epidemic of Epidemics,'" *Vox*, March 6, 2018 (https://www.vox.com/2018/3/6/16453530america-opioid-crisis-epidemic-bacterial-endocarditis-hepatitis-c).

not just OUD treatment, resulting from OUD, after controlling for other health factors. For example, suppose there are two 40-year-old male patients with private insurance. One patient suffers from OUD and the second does not. These analyses compare the health care spending over 12 months for these two patients, starting at the time of the first OUD diagnosis for the individual with OUD. The difference in their health care spending is the excess health care cost attributable to OUD.

50. The cost-of-illness methodology is equipped to capture OUD-related elevated health care costs for diseases other than OUD. Studies of the elevated risk of particular diseases support the finding that health care costs for those with OUD are likely to be higher for a host of reasons. Individuals with OUD that transition to intravenous opioid administration are at elevated risk for transmission of Hepatitis B, C and HIV due to needle sharing and misuse.[73] Opioid users are also at elevated risk of sexually transmitted diseases due to risky behavior.[74] Individuals with OUD are also less likely to take up and adhere to effective contraception and contraceptive care.[75]

51. Data from Cabell County confirm that local experience accords with national research. An HIV cluster was recently identified in Cabell County with 71 cases reported, which represented "a sharp uptick from the baseline average of eight cases annually over the past five years" and represented more cases than in all of West Virginia since 2008.[76] According to the DHHR (Department of Health and Human Services, WV), "The increase reflects a shift in how HIV is being more frequently transmitted, not so much from sexual contact but more so from being passed among intravenous drug users."[77]

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[73] K.M. Rich, *et al.*, "Integrated Models of Care for Individuals with Opioid Use Disorder: How do we Prevent HIV and HCV?" *Current HIV/AIDS Reports*, 15(3), 2018, pp. 266-275; M.R. Golden, *et al.*, "Outbreak of Human Immunodeficiency Virus Infection Among Heterosexual Persons Who are Living Homeless and Inject Drugs – Seattle, Washington, 2018," *Morbidity and Mortality Weekly Report*, 68(15), 2019, p. 344.

[74] D.C. Perlman, D.C. Des Jarlais, and J. Feelemyer, "Can HIV and Hepatitis C Virus Infection be Eliminated Among Persons Who Inject Drugs?" *Journal of Addictive Diseases*, 2015, 34(2-3), pp. 198-205.

[75] R.C. Bowers, *et al*., "Failure of Effective Contraception in Opioid Addicted Mothers: A Disparity in Planned and Actual Usage," *Marshall Journal of Medicine*. 2019, 5(1), pp. 41-49.

[76] See, B. Nash, "DHHR Says Cabell HIV Cluster is Growing," *Charleston Gazette-Mail*, August 12, 2019 (https://www.wvgazettemail.com/news/health/dhhr-says-cabell-hiv-cluster-is-growing/article_ba37b709-32ec-5b16-8b8c-32867037b9b1.html).

[77] *Ibid.*

52. OUD elevated prevalence of infective endocarditis (IE) in the Huntington region. As a 2019 paper reporting data from the Charleston Area Medical Center (a one hour drive from Huntington on I-64) puts it, "One of the potentially lethal and costly complications associated with IV drug use is infective endocarditis (IE)."[78] The number of cases of IV-associated IE at the hospital doubled between 2008 and 2015. Third-party payers cover only part of the average charges of $37,500 for a case.[79] Other regional hospitals have been similarly affected. A report from the University of Cincinnati Medical Center (a 2 hour-40 minute drive from Huntington on Kentucky Route 9) also reports a doubling of IE cases over the period 1999-2009.[80] Using data on payments (rather than charges), the authors found that for the largest payer group, Medicare and Medicaid, the average hospital payment was $95,799. They point out that this figure understates cost because physician fees are not included. Furthermore, IE patients are generally transferred to a skilled nursing facility to complete a typical minimum 6-week course of IV antibiotics.[81] Higher rates of increase in IE have been found in other regions of the country.[82] Dr. Ellen Thompson, a cardiologist at Marshall Health, reports growth of IE cases in Huntington due to IV drug use that match the upward, national trends.[83] Specifically, she reports that IE cases in Cabell Huntington Hospital have increased from 11 in 2010, to 86 in 2018.[84]

53. Table C.II.1 in Appendix C lists studies applying the cost-of-illness methodology to OUD and summarizes their results in terms of estimated excess costs. In one well-known study, Florence, *et al.* (2016) estimate the excess health care costs attributable to OUD for patients with Medicare, Medicaid and private insurance in 2013. They find that health care costs were

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[78] M.C. Bates, *et al*., "Increasing Incidence of IV Drug Use Associated Endocarditis in Southern West Virginia and Potential Economic Impact," *Clinical Cardiology*, 42, 2019, pp. 432-437 at 432.

[79] Calculated from Table 3 of Bates *et al., ibid*. Bates, *et al.* figure that third-party payers covered only 22% of charges overall. Hospital costs are less than charges, but not by that magnitude. In West Virginia, from 2006-2018, the average charge to cost ratio was 40%.

[80] S. Keeshin and J. Feinberg," Endocarditis as a Marker for New Epidemics of Injection Drug Use," *American Journal of the Medical Sciences*, 352(6), December 2016, pp. 609–614.

[81] *Ibid.*

[82] A. Fleischauer, *et al.*, "Hospitalizations for Endocarditis and Associated Health Care Costs Among Persons with Diagnosed Drug Dependence – North Carolina, 2010–2015," *Morbidity and Mortality Weekly Report*, 66 (22), June 9, 2017, pp. 569-573.

[83] Expert Report of Ellen Thompson, M.D., August 3, 2020, p. 2.

[84] *Ibid.*

$15,500 higher for commercially insured patients, $17,052 higher for Medicare patients, and $13,743 higher for Medicaid patients.[85] A recent study by Leslie, *et al.* (2019) estimates the excess health care costs for Medicaid patients for each year from 1999 through 2013.[86] Another recent study sponsored by the Society of Actuaries estimates excess costs for Medicaid as well as other major payers over the period 2015-2018.[87] I primarily rely on these later two studies to quantify excess health care costs due to OUD.

54. Table 5 reports the number and valuation of excess health care costs attributed to sales and distribution of prescription opioid products in Cabell County from 2006-2018. Total morbidity costs are the product of the share of OUD cases in each of the two major payer categories (Medicare/Commercial in the second row and Medicaid/Uninsured in the third row of Table 5) and their respective excess health-cost estimates (rows 4 and 5 of Table 5). Over this time period, the measure of the economic cost of excess health care use is over $501 million for Cabell County.

[85] Florence, *et al.*, *op. cit.*, Table 2.

[86] D. Leslie, *et al.*, "The Economic Burden of the Opioid Epidemic on States: The Case of Medicaid," *American Journal of Managed Care*, June 2019, Supplement 25(13), pp. S243-249.

[87] Davenport, *et al.*, *op. cit.*

Table 5
Morbidity and Excess Health Care Costs Attributed to the Sales and Distribution of Prescription Opioids
Cabell County, 2006-2018

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
Total OUD cases due to prescription opioids	3,859	5,952	3,433	3,773	4,985	6,230	3,530	7,218	6,020	7,240	7,148	9,018	7,109	75,515
Share of OUD cases covered by Medicare/Commercial payers	43.6%	39.0%	43.8%	43.8%	39.3%	40.9%	38.9%	37.7%	34.9%	34.5%	34.4%	32.0%	32.0%	
Share of OUD cases covered by Medicaid/Uninsured	56.4%	61.0%	56.3%	56.3%	60.7%	59.1%	61.1%	62.3%	65.1%	65.5%	65.6%	68.0%	68.0%	
Excess health care costs per OUD case covered by Medicare/Commercial payers	$13,567	$12,914	$11,761	$11,781	$12,017	$10,866	$10,344	$8,878	$8,878	$8,878	$8,878	$8,878	$8,878	
Excess health care costs per OUD case covered by Medicaid/Uninsured	$6,044	$5,753	$5,240	$5,249	$5,354	$4,841	$4,609	$3,955	$3,955	$3,955	$3,955	$3,955	$3,955	
Total excess health care costs due to prescription opioids ($ mil)	**$36.0**	**$50.9**	**$27.8**	**$30.6**	**$39.8**	**$45.5**	**$24.2**	**$41.9**	**$34.2**	**$40.9**	**$40.4**	**$49.9**	**$39.3**	**$501.3**

Source: Keyes Report, Figure 14 and Appendix C, Tables C.II.4 and C.II.5

55. My valuation of the excess cost of health care treatment for people with OUD due to prescription opioids underestimates the full cost of OUD morbidity to the Cabell Huntington Community. Local governments, partly with grant support, community organizations, and in some cases private citizens, pay for health care and other social services. Programs in Huntington include the Provider Response Organization and Addiction Care and Treatment (PROACT), a facility that provides housing, social and clinical support, as well as Medication for Opioid Use Disorder (MOUD)[88] for its patients.[89] Drug overdoses strained first-responders' capacity.[90] Figures 4a and 4b, taken from material prepared by Scott Lemley, the Executive Director of the Department of Development and Planning at the City of Huntington, and

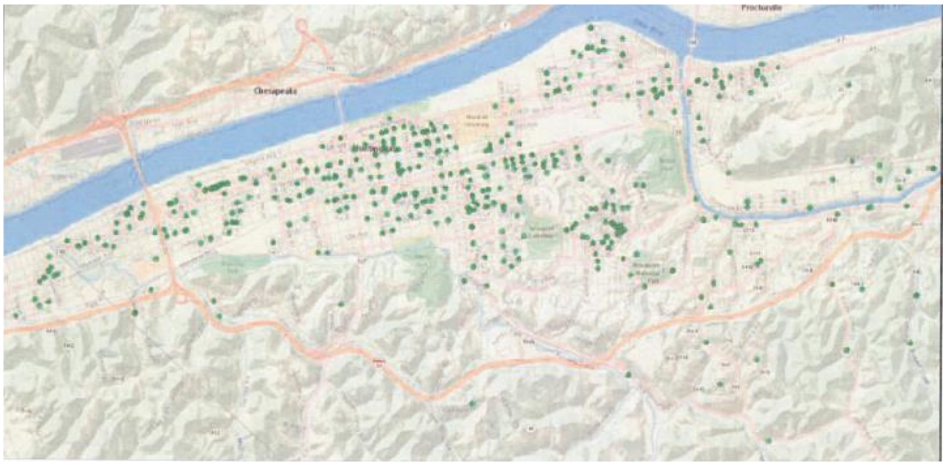
[88] MOUD was formerly referred to as MAT (Medically Assisted Treatment). See National Council for Behavioral Health, "Medication-Assisted Treatment (MAT) for Opioid Use Disorder in Jails and Prisons," January 2020d (https://www.thenationalcouncil.org/medication-assisted-treatment-for-opioid-use-disorder-in-jails-and-prisons/).

[89] The City of Solutions, Huntington WV, pp. 39-40.

[90] "...overdoses were a big issue. Responding to them, I think they felt -- I don't want to say 'helpless,' but first responders are problem solvers, and I think they felt like it was a problem they couldn't solve, and again, it caused compassion fatigue, burnout…" (Lemley Deposition, p. 31).

previously a Crime Intelligence Analyst for the Huntington Police Department, are maps showing the incidents and concentration of non-fatal drug overdoses in Huntington in one year, 2016. Lemley explains regarding the two figures: "So you have a dot every time there was an incident of a nonfatal overdose. And … it gets kind of tricky because you have dots on top of dots on top of dots if they're at the same address, so it can be difficult to see, which is why we did the heat map, as we say, showing concentrations."[91] On the heat map the red areas have higher concetrations than the yellow and green areas.

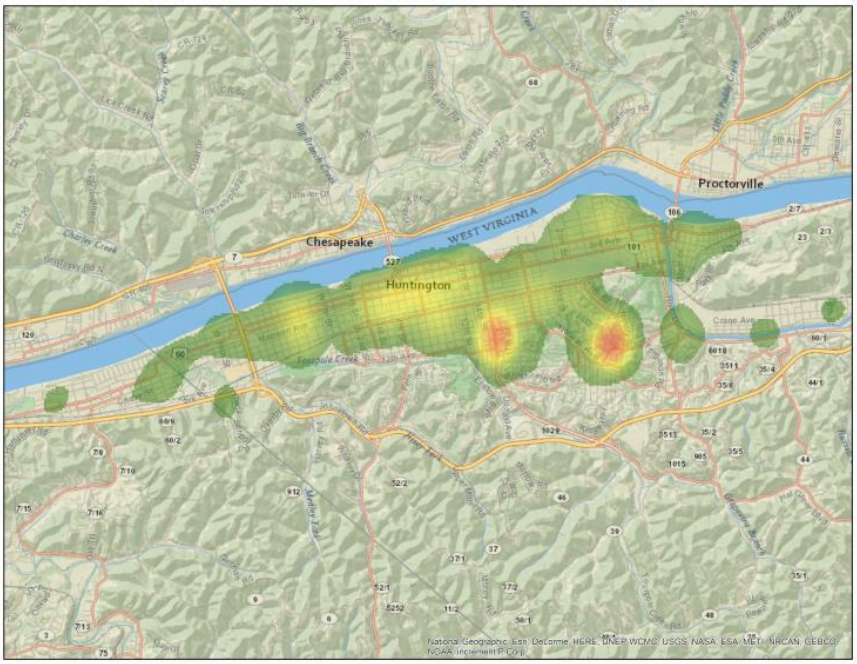
Figure 4a
Incidence Map: Non-Fatal Drug Overdoses in Huntington, 2016[92]



[91] Lemley Deposition, pp. 330-333, quote from p. 333. Referencing Deposition Exhibit 1. The exhibit, "The Huntington Model: How One West Virginia City is Fighting Back Against Opioids," also includes data on the number of nonfatal overdoses in Cabell County for 2015 (874 cases) and 2016 (1,404 cases).

[92] Note that these overdoses include prescription and non-prescription opioids.

Figure 4b
Heat Map: Non-Fatal Drug Overdoses in Huntington, 2016[93]



Prescription Opioids and Workforce Productivity

56. Pain from injury can interfere with an individual's ability to work,[94] and reductions in pain enable some to work who would have otherwise been prevented from working due to pain.[95] A study of the effects of Cox-2 inhibitors (non-opioid pain medications) finds that treatment increases workplace attendance.[96] Opioids are medically indicated for severe pain associated

[93] Note that these overdoses include prescription and non-prescription opioids.

[94] D.J. Gaskin and P. Richard, "The Economic Cost of Pain in the United States," *Journal of Pain*, 13(8), 2012, pp. 715-724.

[95] Participation in the labor force benefits the individual and the wider society. The individual benefits to the degree that added income adds to their consumption opportunities. Others benefit to the degree that the added income of the worker increases public tax revenue or offsets costs others would have paid to support consumption of the individual had they been out of the labor force. For example, those outside of the labor force are paid unemployment or disability benefits; avoiding these transfer payments benefits the public. Support for an individual out of the labor force may come from other family members, and this support is not needed if an individual is working and supporting themselves. In other words, how much of the benefits of labor force participation flow directly to the worker or to others depends on the individual circumstances.

[96] Cox-2 inhibitors are not generally used for recreational purposes. See C. Garthwaite, "The economic benefits of pharmaceutical innovations: The case of cox-2 inhibitors," *American Economic Journal: Applied Economics*, 4(3), 2012, pp. 116-137. A. Butikofer and M. M. Skira, "Missing Work is a Pain: The Effect of Cox-2 Inhibitors on Sickness Absence and Disability Pension Receipt," *Journal of Human Resources*, 53(1), 2018, pp. 71-122.

with trauma, post-surgery, and cancer end-of-life care, conditions for which pain reduction may not have a large effect on labor force participation.[97] Nonetheless, it is at least theoretically possible that in some instances, additional appropriate opioid prescriptions could increase productivity.

57. Prescription opioids are associated with numerous adverse consequences with increasing dose and duration of use, including development of OUD but also death, morbidity, crime, incarceration, and child maltreatment, all of which decrease labor force participation of the user and/or of others in the immediate and longer term. A working paper from the National Bureau of Economic Research studied the effect of opioid prescriptions on workers out on temporary disability with low-back pain. Long-term treatment with opioids increased the length of time workers missed work due to disability.[98]

58. Some recent papers in the economics literature study the effect of opioid prescriptions on a geographic basis (rather than for populations who might be candidates for appropriate treatment), and thus capture empirically both the positive effects (from worker pain treatment) and some negative effects (from inappropriate treatment) of opioid prescriptions on work.[99] As one set of authors put it, "Because it is impossible to distinguish between legitimate and illegitimate uses of prescription opioids, we interpret these [geographic-level] results as a net effect of both types of use."[100] These authors found that the net effect of prescribing on

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[97] Lembke Report, Appendix IV, p.253. Further, CDC provides guidance on the use of prescription opioids for pain relief outside of palliative, cancer, or end-of-life care. These guidelines recommend the use of non-opioid analgesics for chronic pain management and emphasize patient safety from addiction. See D. Dowell, T.M. Haegerich, and R. Chou, "CDC Guidelines for Prescribing Opioids for Chronic Pain – United States, 2016," *JAMA*, 315(15), 2016, pp. 1624-1645.

[98] B. Savych, D. Neumark and R. Lea, "Do Opioids Help Injured Workers Recover and Get Back to Work? The Impact of Opioid Prescriptions on the Duration of Temporary Disability," National Bureau of Economic Research, Cambridge, MA, April 2018.

[99] M.C. Harris, *et al.*, "Prescription Opioids and Labor Market Pains: The Effect of Schedule II Opioids on Labor Force Participation and Unemployment," working paper, March 28, 2018, pp. 1-44 at p. 1 (https://mpra.ub.uni-muenchen.de/86586/1/MPRA_paper_86586.pdf); A. Krueger, "Where Have All the Workers Gone? An Inquiry into the Decline of the U.S. Labor Force Participation Rate," Brookings Papers on Economic Activity, 2017; and J. Currie, J. Jin, and M. Schnell, "U.S. Employment and Opioids: Is There a Connection?" in *Health and Labor Markets*, Research in Labor Economics, Volume 47, 2019, Emerald Publishing Limited.

[100] Harris, *et al., op. cit.*

productivity at the state level was negative.[101] One paper using county data on prescription rates and employment by age and gender finds that a higher rate of prescriptions has a small positive effect on employment for women, but no effect on men.[102] Finally, a recent paper finds that increasing prescription opioid prescribing rates decreases the prime-age employment rate for both men and women.[103]

59. A paper sponsored by the American Action Forum can be used as a basis for quantifying the loss in output associated with prescription opioids. Krueger found that areas with higher opioid prescription rates have lower rates of labor force participation overall.[104] A follow up analysis by the Forum updated the Krueger paper and calculated the reduction in workforce and output for each state.[105] West Virginia was among the hardest hit states because of the massive state-wide growth in opioid prescriptions.[106] According to the report, the largest negative economic effects in the country occurred in Arkansas and West Virginia, "where the prime-age labor force participation rate declined by 3.8 percentage points and the real economic growth rate slowed by 1.7 percentage points." This research, and the others mentioned in this and the previous two paragraphs, are summarized and compared in more detail in Table C.II.7 of Appendix C.

60. On the basis of the available evidence, I am of the opinion that the net effect of the sales and distribution of prescription opioids on labor productivity is negative: more prescriptions

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[101] Harris, *et al.*, *op. cit.* study ten states using data from Prescription Drug Monitoring Programs and find that a 10% increase in per capita prescriptions leads to a 0.56 percentage point decrease in labor force participation.

[102] Currie, Jin, and Schnell, *op. cit.*

[103] D. Aliprantis, K. Fee, and M.E. Schweitzer, "Opioids and the Labor Market," *Federal Reserve Bank of Cleveland*, Working Paper No. 18-07, 2019.

[104] Krueger, *op. cit.*

[105] American Action Forum, "State-By-State: The Labor Force and Economic Effects of the Opioid Crisis," September 12, 2018 (https://www.americanactionforum.org/project/opioid-state-summary/west-virginia/). The new report also corrects for an interpretation error in the original Krueger analysis associated with non-linear properties of his regression specification. When the interpretation is corrected, "the regression indicates that growth in opioids led the nationwide prime-age labor force participation rate to decline by 1.4 percentage points for men (40 percent of the total decline) and 1.8 percentage points for women (nearly 60 percent of the total decline)." This effect is about twice as large as contained in Krueger's analysis.

[106] The CDC has IQVIA data on per-capita opioid prescribing rates. From 2006-2011, West Virginia had the highest rate in the nation. From 2012-2014, it had the second highest rate; in 2015, the fourth. In 2016 and 2017, it was the 8th highest. See CDC, "U.S. Opioid Prescribing Rate Maps" (https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html) for data and details.

mean less work. This conclusion is bolstered by the observation that the short-term harms of the sales and distribution of prescription opioids on workforce productivity underestimate the full negative effects which play out over time. A worker who develops OUD today because of prescription opioids may have reduced labor-force participation, on average, for years to come.

61. Experience in the Community accords with the research studies. I have not undertaken a quantification of the longer-term effects on productivity from the sales and distribution of prescription opioids (apart from death, criminality, and child maltreatment). But given the dynamics of opioid use and OUD, measurement of these longer-term effects on productivity from sales and distribution of prescription opioids would result in a much greater imbalance where the costs far exceed the benefits in productivity.

62. The overall purpose of my analysis here is to determine whether overall costs from the sales and distribution of prescription opioids exceed ostensible benefits. As a result, if a particular quantification is not needed to make that determination, I can simplify the analysis by making conservative assumptions. Therefore, even though I believe costs to workforce productivity outweigh the benefits, when counting and valuing the effects of prescription opioids on workforce productivity, I will conservatively treat the positive and negative as approximately canceling out.

63. My opinion that the costs of prescription opioids in terms of workforce participation outweigh the potential benefits is complemented by the opinions of medical experts regarding the clinical costs and benefits. Dr. Lembke, a physician who has treated many patients with OUD, addresses the issue of benefits of prescription opioids in relation to alternative treatments and concludes that "the best available evidence … found that non-opioid medications (NSAIDs, acetaminophen) provide equivalent or greater pain relief, while opioids confer significantly greater risks …"[107] Dr. Lembke also discusses a systematic literature review which concludes that prescription opioids fare poorly even in relation to placebo (*i.e.*, no) treatment. The review found "that the difference in pain relief did not meet a pre-specified

[107] Lembke Report, pp. 254 – 255.

'Minimally Important Difference' (MID), that is, 'the smallest amount of improvement in a treatment outcome that patients would recognize as important.'"[108]

64. Dr. Lembke states:[109]

> "Based on the consensus view stated in the NASEM [National Academies of Sciences, Engineering, and Medicine] Report, research findings, and my own clinical experience, it is my view that **at a population level**, the risks of long-term opioids for chronic pain far outweigh the benefits. For very few patients, benefits might outweigh the risks; but even then risks increase with higher dose and longer duration of opioid treatment, such that risks may eventually exceed any small possible benefit over other less dangerous pain reduction strategies." (emphasis added)

65. Dr. Lembke goes on to state her conclusions as follows:[110]

> "The adverse effects of opioids are well-known and devastating. These include overdose mortality, primarily due to respiratory suppression; non-fatal overdose; OUD; and neonatal abstinence syndrome (NAS), which afflicts newborns well into childhood. These conditions are severe, fatal or life-threatening, permanent or of long duration. The Cabell Huntington Community has been even more severely impacted than the US as a whole.
>
> In contrast, the benefits of prescription opioids are limited or ephemeral. I agree with the consensus of leading authorities that there is no reliable evidence that long-term opioids provide clinically significant relief of CNCP, and the best evidence supports equivalent pain relief and fewer risks with non-opioids such as NSAIDs. Although opioids are indicated for acute pain, numerous studies show equivalent relief and lower risk with non-opioids; a significant minority of acute-pain opioid patients go on to become persistent users who suffer dependency but do not benefit from opioid use; over-prescribing for acute conditions results in diversion to inappropriate users, a source of community harm that further offsets any pain relief benefits to appropriate users; and the pain relief in acute conditions is inherently brief, compared to the long-term or permanent harms of fatal and non-fatal overdose, OUD and NAS.
>
> In summary, it is my clinical opinion that the harms of prescription opioids to the Cabell Huntington Community far outweigh any benefits that may be conferred."

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[108] Lembke Report, p. 254. See J.W. Busse, *et al.*, "Opioids for Chronic Noncancer Pain: A Systematic Review and Meta-Analysis," *JAMA*, 320(23), 2018, pp. 2448-2460.

[109] Lembke Report, p.255. Dr. Lembke's reference in this quotation is to: National Academies of Science Engineering and Medicine (NASEM), "Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use," 2017, p. 51.

[110] Lembke, Appendix IV, p. 261.

66. See also the Report of Dr. Waller, a practicing addiction, pain, and emergency medicine physician, where he discusses the limited clinical situations in which opioids are a medically appropriate option, and the very substantial medical risk incurred by prescription opioid use.[111]

C. Babies Born with Neonatal Abstinence Syndrome (NAS)

Overview

67. Neonatal abstinence syndrome (NAS), also termed neonatal withdrawal,[112] is a constellation of conditions associated with *in utero* exposure to opioids.[113] It can occur due to any regular antenatal opioid use, including whether opioids are taken as prescribed or non-medically.[114] According to the CDC, "Neonatal abstinence syndrome (NAS) is a postnatal drug withdrawal syndrome in newborns caused primarily by *in utero* exposure to opioids."[115]

68. The syndrome is a rapidly growing public health problem, with the incidence of NAS increasing dramatically between 2000-2012, corresponding with a rise in opioid use and abuse.[116] Babies born with NAS may exhibit a host of symptoms, including respiratory distress;

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[111] Expert Report of Dr. Corey Waller, in this matter, August 3rd, 2020 (hereafter Waller Report). Dr. Waller rejects opioids as an appropriate treatment choice for chronic pain management and considers them a risky treatment course in intra-operative and post-surgical settings, concluding that "…except for pain treatment in severe acute trauma, palliative care, and hospice treatment, opioids should be considered the approach of last resort when treating patients with acute or chronic pain (p. 40)." Dr. Waller characterizes palliative care and hospice as the "core scope under which opioids may be used appropriately" (p. 39). "Balancing opioids' severe risks with the lack of efficacy of opioids to treat chronic pain makes it obvious that opioids are of little to no use in chronic pain and should be used sparingly, if at all, to treat pain lasting more than 3-7 days" (p. 39). In page 23 of his report, Dr. Waller describes the "serious, severe and predictable" risks associated with the drugs at issue in this matter: "addiction, dependence, tolerance, withdrawal, respiratory depression, overdose, and death"

[112] K. McQueen and J. Murphy-Oikonen, "Neonatal Abstinence Syndrome," *New England Journal of Medicine,* 375(25), 2016, pp. 2468-2479.

[113] H. Uebel, *et al.*, "Reasons for Rehospitalization In Children Who Had Neonatal Abstinence Syndrome," *Pediatrics,* 136(4), 2015, pp. e811-e820.

[114] S. Wong, *et al.*, "Substance Use in Pregnancy," *Journal of Obstetrics and Gynecology Canada*, 33(4), 2011, pp. 367-384.

[115] CDC, "Incidence of Neonatal Abstinence Syndrome – 28 States, 1999-2013," Morbidity and Mortality Weekly Report (MMWR), 65(31), August 12, 2016, pp. 799-802 at p. 801 (https://www.cdc.gov/mmwr/volumes/65/wr/mm6531a2.htm).

[116] S.W. Patrick, *et al*., "Neonatal Abstinence Syndrome and Associated Health Care Expenditures: United States, 2000-2009," *JAMA*, 307(18), 2012, pp. 1934-1940; S.W. Patrick, *et al.*, "Increasing Incidence and Geographic Distribution of Neonatal Abstinence Syndrome: United States 2009 to 2012," *Journal of Perinatology*, 35(8), August 2015, pp. 650-655.

central nervous system symptoms like tremors and seizure; and gastrointestinal problems such as poor feeding and vomiting.[117] The onset of symptoms typically occurs within the first few days following birth.[118]

69. Calculating the harm from babies born with NAS in the Cabell Huntington Community and attributable to prescription opioids is based on multiplying the number of NAS cases due to prescription opioids by the economic costs associated with an NAS birth. I consider three types of excess economic costs due to NAS: hospital costs at birth, health care costs during childhood, and special education costs. I describe the rationale for each of these cost categories below.

70. The NAS epidemic has prompted a forceful response from the Cabell Huntington Community. One example is Lily's Place, which opened in Huntington in October 2014.[119] Lily's place "provides short-term medical care to infants suffering from prenatal drug exposure and offers non-judgmental support, education, and counseling to families," and has become a regional and national resource for care of NAS babies.[120] NAS babies come to Lily's Place directly after leaving the hospital. Lily's Place spends more than $1 million caring for infants with NAS each year since 2016.[121]

71. Figure 7 compares the NAS rate in Cabell County to the West Virginia and national rates, which are supplied by Professor Keyes.[122] West Virginia has a much higher rate than the nation overall, and Cabell has a rate higher still than the West Virginia average rate. Between 2013 and 2015, the rate of NAS births was more than 500% greater in Cabell County than nationwide.

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[117] S. Wong, *et al.*, *op. cit.*, Table 6.

[118] S. Wong, *et al.*, *op. cit.*, p. 375.

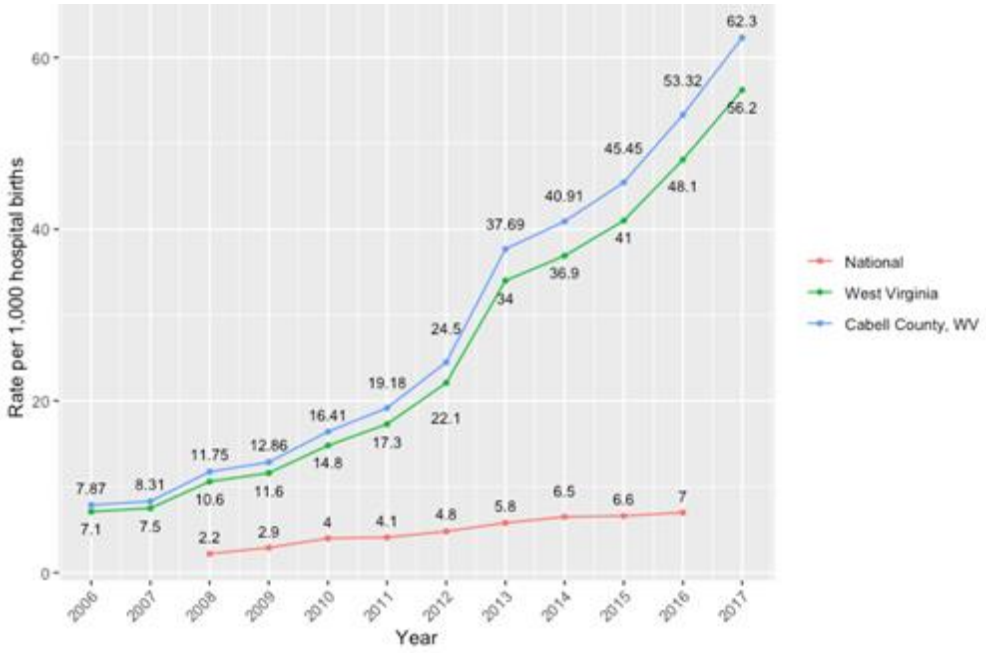
[119] Lily's Place, Inc., Annual Financial Report, 2017 (HUNT_00197045-55 and https://lilysplace.org/about). See also, The City of Solutions, Huntington WV, pp. 43-44.

[120] Lily's Place, *op. cit.*, p. 6.

[121] Financial details of Lily's Place come from ProPublica's nonprofit Explorer (https://projects.propublica.org/nonprofits/organizations/462235123). In, 2017, for example, Lily's Place spent $1.2 million.

[122] Keyes Report, Figure 10.

Figure 7
NAS Cases per 1,000 Hospital Births
National, West Virginia and Cabell County Rates
Replication of Keyes Report, Figure 10



Count of Births with NAS

72. To identify the number of NAS babies in Cabell County, I rely on Professor Keyes. Professor Keyes states: "The majority of neonatal abstinence syndrome among US infants is due to opioid exposure in utero."[123] On this basis I conservatively attribute 50% of her estimated number of NAS births in Cabell County to opioids.[124] She provides estimates of the number of NAS births attributable to opioid use for the years 2006-2015, but not for 2016-2018 due to data unavailability. To estimate to the number of NAS births attributable to prescription opioids, I assume the share of NAS births due to prescription opioids is the same as the share of OUD due to prescription opioids. Specifically, I use the last row from Table 4 above to determine the number of NAS births due, directly or indirectly, to prescription opioids. Table 6 presents the counts for NAS due to prescription opioids in Cabell County.

[123] Keyes Report, p. 36.

[124] Keyes Report, Table 1.

Table 6
NAS Births Due to Prescription Opioids in Cabell County
2006-2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Total
Cabell County NAS cases	10.0	10.0	15.0	16.0	19.0	23.0	30.0	44.0	46.0	49.0	262.0
Cabell County NAS cases due to opioids	5.0	5.0	7.5	8.0	9.5	11.5	15.0	22.0	23.0	24.5	131.0
Share of NAS cases due to prescription opioids	97%	97%	99%	99%	98%	98%	94%	94%	90%	88%	
Cabell County NAS cases due to prescription opioids	4.9	4.9	7.4	7.9	9.3	11.3	14.1	20.6	20.7	21.5	122.6

Sources: Keyes Report, Table 1, and Table 4 above.

Valuation of Excess Costs of NAS

73. A baby born with NAS is more likely to have elevated health care costs at birth,[125] higher levels of morbidity and rehospitalization through childhood,[126] increased risk of educational disability,[127] development delay,[128] and poor school performance.[129] NAS births are associated with more intensive hospital utilization than other births, including, for example, increased length of stay and increased risk of transfer to the neonatal intensive care unit, resulting in higher costs.[130] Later in life, children born with NAS are more likely to suffer mental and physical trauma, endure maltreatment, develop ophthalmologic conditions, behavioral disorders, and

[125] S.W. Patrick, *et al.*, *op. cit.*; American College of Obstetricians and Gynecologists, "Opioid Use and Opioid Use Disorder in Pregnancy. Committee Opinion No. 711," *Obstetrics & Gynecology*, 130(2), 2017, pp. e81-e94.

[126] G. Liu, *et al.*, "A Longitudinal Healthcare Use Profile of Children with A History of Neonatal Abstinence Syndrome," *The Journal of Pediatrics*, 204, 2019, pp. 111-117.

[127] M.M. A Fill, *et al.*, "Educational Disabilities Among Children Born with Neonatal Abstinence Syndrome," *Pediatrics*, 142(3), 2018, p. e20180562.

[128] E.S. Hall, J.M. McAllister, and S.L. Wexelblatt, "Developmental Disorders and Medical Complications Among Infants with Subclinical Intrauterine Opioid Exposures," *Population Health Management*, 22(1), 2019, pp. 19-24.

[129] J.L. Oei, *et al.*, "Neonatal Abstinence Syndrome and High School Performance," *Pediatrics*, 139(2), 2017, p. e20162651.

[130] S. Wong, *et al.*, *op. cit.* See also: T.E. Corr and C.S. Hollenbeak, "The Economic Burden of Neonatal Abstinence Syndrome in the United States," *Addiction*, 112, 2017, pp. 1590-1599.

suffer preventable injuries that require care and in some cases repeat hospitalizations.[131] I focus on excess health care costs during childbirth and childhood, and excess costs incurred for special education. Data are not available for excess costs later in life.

74. I begin with excess hospital costs associated with an NAS delivery. Hospital discharge data reports "charges," a form of list price that is generally not what health care payers actually pay. To quantify the excess hospital costs due to NAS, I begin with the difference between the average hospital charge for an NAS case in West Virginia and the average hospital charge for all births[132] in the state in each year. I then convert excess hospital charges to excess hospital costs by multiplying charges by net revenue-to-charge ratios from the American Hospital Association. This adjustment, in effect, transforms charges into costs to payers (which equals revenue to the hospital). Table 7 reports the total estimated hospital costs of NAS attributable to prescription opioid sales; these costs were over $1.4 million in Cabell County between 2006-2015. See Appendix C Section III for information about the estimate of hospital costs.

[131] H. Uebel, *et al.*, *op. cit.* Professor Keyes discusses the adverse downstream consequences at length in her report (Keyes Report, p. 36).

[132] Note that the average charge for all births include charges for NAS making my calculation conservative as NAS-related charges are higher than non-NAS related charges.

Confidential

Table 7
Neonatal Abstinence Syndrome (NAS) and Valuation
Due to Sales and Distribution of Prescription Opioids
Cabell County, 2006-2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Total
NAS cases in Cabell County	10.0	10.0	15.0	16.0	19.0	23.0	30.0	44.0	46.0	49.0	262.0
NAS cases attributed to prescription opioids	4.9	4.9	7.4	7.9	9.3	11.3	14.1	20.6	20.7	21.5	122.6
Excess hospital costs for NAS births	$11,083	$10,848	$15,785	$34,357	$56,742	$109,151	$199,535	$266,558	$316,755	$375,693	$1,396,506
Excess child health care cost for NAS cases	$44,413	$44,422	$67,520	$72,024	$84,802	$102,671	$128,228	$188,127	$188,971	$195,764	$1,116,943
Excess special education costs for NAS cases	$3,533	$3,534	$5,372	$5,730	$6,747	$8,168	$10,202	$14,967	$15,034	$15,575	$88,862
Total NAS excess costs due to prescription opioids ($million)	**$0.06**	**$0.06**	**$0.09**	**$0.11**	**$0.15**	**$0.22**	**$0.34**	**$0.47**	**$0.52**	**$0.59**	**$2.60**

Sources: Keyes Report, Table 1 and Appendix C, Tables C.III.1 - C.III.3

75. Turning to excess health care costs during childhood due to NAS, Liu, *et al.* find, in a privately insured national population in 2005-2014, that children ages 1-8 born with NAS incur an average of $6,927 per year in health care costs, compared to $2,735 for those without, implying an annual excess health care cost of $4,192 for children born with NAS.[133] Most children born with NAS are covered by Medicaid.[134] I adjust the Liu, *et al.* estimates downward to reflect lower Medicaid costs and lower costs in West Virginia using the same approach as in the morbidity section above.[135] Applying these adjustments to determine an annual excess health care cost for children born with NAS in West Virginia, and then multiplying by 8 years for years yields excess health care costs of $9,113 per child with NAS. This estimate is conservative in that the health care costs from the Liu, *et al.* study include earlier years than the 2006-2015 years

[133] G. Liu, *et al*, *op. cit.* These costs include hospitalizations, emergency department visits, outpatient evaluations, and prescription drugs.

[134] S.W. Patrick, *et al*, *op. cit.*

[135] Medicare/Commercial costs for OUD were 224.5% higher relative to Medicaid/Uninsured. Moreover, West Virginia Medicaid costs for OUD were 39% lower than the national average.

addressed in my Report. These excess health care costs amount to $1.1 million from 2006-2015 in Cabell County.

76. Children born with NAS are also more likely to incur additional educational expenses, in the form of evaluation for disabilities, use of speech or other developmental therapy, and other services.[136] Fill, *et al.* estimate that children with NAS in Tennessee are 3.9 percentage points more likely to receive special education services and therapy (15.3% versus 11.4%).[137] Based on the academic literature, I estimate that the average cost of services provided to special education students is approximately $9,298 per year.[138] Students receive an average of two years of special education.[139] Multiplying these variables results in an estimate of $725 in average excess educational cost per student with NAS.[140] These costs add $0.09 million to the total costs to the Cabell Huntington Community attributable to prescription opioids over the years 2006-2015. See Appendix C Section III for a detailed description of methods and sources used for these calculations.

77. My valuation of the cost of NAS is conservative. First, as explained above, data are not available to provide estimates for the years 2016-2018. Figure 7 above shows a steep, upward trend in the NAS rate in Cabell County, in parallel to West Virginia. This suggests that the NAS rate in Cabell County would also have gone up over these latter years. My valuation does not include some costs after the baby is discharged from the hospital, including Cabell Huntington Community efforts for children born with NAS and their families. Furthermore, because of data limitations, I omit some categories of excess costs due to NAS. For example, children born with NAS have worse health outcomes into early adulthood.[141] Higher health care costs might persist

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[136] J.L. Oei, *et al., op. cit.*

[137] M.M.A. Fill, *et al., op. cit.*

[138] See Appendix C for details on how I derive this valuation.

[139] E.W. Holt, D.J. McGrath, and W.L. Herring, "Timing and Duration of Student Participation in Special Education in the Primary Grades," NCES, 2007-043, Washington DC, National Center for Education Statistics, 2007.

[140] ($9,298) * 2 * 0.039 = $725.

[141] H. Uebel, *et al., op. cit.*

after age 8,[142] but I am not aware of research on which to base a quantitative calculation of ongoing excess health care costs. Evidence suggests that children born with NAS have lower educational outcomes later in life and underperform in school.[143] The positive relationship between education and income is well-known, implying a cost to the children in terms of lower income, fewer economic opportunities and reduced upward mobility.[144] Moreover, education levels are inversely correlated with participation in criminal activities, and drug use.[145] Finally, the long-term adverse consequences of NAS are unknown and as such there are no data of which I am aware to quantify the long-term economic damages to a generation with so many babies born with NAS.

D. Crime

Overview

78. The sales and distribution of prescription opioids increase crime through a number of causal channels. For example, the resale of prescription opioids (*e.g.*, OxyContin) is a crime. Additionally, people misusing opioids may commit crimes, such as property theft, to obtain money to buy opioids or their drug use may lead to other crimes, such as assault.[146]

79. My approach for valuing the economic harm of criminal activity in the Cabell Huntington Community due to prescription opioids is as follows. First, I obtain local crime data, from which

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[142] Two literature reviews find scant research on the longer-term consequences from children born with NAS. See D.J. Maguire, S. Taylor, K. Armstrong, *et al.*, "Long-Term Outcomes of Infants With Neonatal Abstinence Syndrome," *Neonatal Network*, 35(5), 2016, pp. 277-286 and H.J. Harder and A.Z. Murphy, "Early Life Opioid Exposure and Potential Long-Term Effects," *Neurobiology of Stress*, 10, 2019, p. 100156.

[143] J.L. Oei, *et al., op. cit.*

[144] D. Card, "The Causal Effect of Education on Earnings," *Handbook of Labor Economics*, 3, Elsevier, 1999, pp. 1801-1863.

[145] L. Lochner and E. Moretti' "The Effect Of Education on Crime: Evidence From Prison Inmates, Arrests, and Self-Reports," *American Economic Review*, 94(1), 2004, pp. 155-189; P. Chatterji, "Illicit Drug Use and Educational Attainment," *Health Economics*, 15(5), 2006, pp. 489-511.

[146] T.N.A. Winkelman, V.W. Chang, and I.A. Binswanger, "Health, Polysubstance Use, and Criminal Justice Involvement Among Adults with Varying Levels of Opioid Use," *JAMA Open Network*, 1(3), 2018, pp. e180558-e180558; R. N. Hansen, *et al*., "Economic Costs of Nonmedical use of Prescription Opioids," *The Clinical Journal of Pain*, 27(3), 2011, pp. 194-202.

I derive a share of crime due to prescription opioids. Second, I take these counts and multiply by crime cost valuations from the research literature based on the type of offense.

80. In Huntington, local officials attest that opioids drive crime. In 2017, in reporting in *The Herald Dispatch* by Courtney Hessler, Captain Hank Dial stated that many of the city's crime problems "stem from drug trafficking ..."[147] In other reporting by Hessler in *The Herald Dispatch*, according to Chief of Police Joe Ciccrelli: "If you aren't involved in drugs, the chance of being a victim of violent crimes is pretty slim ..."[148] The Chief went on to say, "It's common we have drug robberies…. When we say the victim isn't cooperating, there's a reason. They will take their licks and go on. Oftentimes, there are retaliation shootings."[149] City of Huntington Mayor Williams was aware of this relationship years before. When asked as to his awareness of an opioid problem prior to 2014, he responds: "The City had a problem with several different drugs. In 2014, I became aware that opioids was more than just a problem; that it was driving … the extent of the drug trade, the crime and other problems within the City. And that's when … I received a heightened awareness of the extent of the opioid epidemic."[150]

81. Drug crimes in the Cabell Huntington Community increased dramatically in step with the opioid epidemic. Figures 8a and 8b depict the "hot spots" of drug offenses for 2004 and 2014 in Huntington. High-crime areas got hotter, and the heat spread throughout the city over this ten-year period.[151] In his deposition, Scott Lemley, creator of the heat maps, describes what they show: "What you see in 2004 was in the Fairfield neighborhood. It was known for dealing of drugs, drug possession, violent crimes… as you move from 2004 to '14, it literally went from a

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[147] J. Qualls, and C. Hessler, "Leaders Address Public Safety Concerns with 'Show of Force,'" *The Herald-Dispatch*, December 13, 2017 (www.herald-dispatch.com/_recent_news/leaders-address-public-safety-concerns-with-show-of-force/article_355de5bc-dfb1-11e7-be5a-c7043283e7a3.html?fbclid=IwAR3YrbSmcAq QkODyZCS4IGZWe2T5CVEdZQ_wIyRLQfP_1jD5YF5dd4tVIJQ#utm_campaign=blox&utm_source=facebook&utm_medium=social).

[148] C. Hessler, "Violent Crime Rate in City Grew in 2016," *The Herald-Dispatch*, March 12, 2017 (www.herald-dispatch.com/news/violent-crime-rate-in-city-grew-in-2016/article_44a5b63f-cc4e-56b0-a7b6-db3fbfe4d70f.html).

[149] *Ibid.*

[150] Deposition of Steve Williams, in this matter, June 30, 2020 (hereafter Williams Deposition), p. 24.

[151] Lemley Deposition, pp. 329-330.

very small area to touching almost every neighborhood in Huntington…it permeated from a geographic standpoint, everywhere." [152]

Figure 8a
Drug Offenses Heat Maps, Huntington
2004

Figure 8b
Drug Offenses Heat Maps, Huntington
2014

[152] *Ibid.*

82. In response to the wave of criminal activity due to drugs, the Huntington Mayor's Office of Drug Control and Policy was established to fight the harm due to drug addiction in Huntington.[153] The office enhances ties with federal law enforcement agencies, and promotes surveillance of drug dealers through the justice system.

83. As noted above at ¶¶ 29 and 35, the valuation of crimes presented here based on the research literature does not include a measure of the stress imposed on first responders among the police, fire and EMS units.

Count of Crimes

84. I start with a count of the total number of crimes in different categories, (*e.g.*, motor vehicle theft, prostitution, vandalism) committed within the Cabell Huntington Community, based on reports from law-enforcement agencies (LEAs) covering the Community. Counts of incidents come from the National Incident-Based Reporting System (NIBRS) maintained by the FBI. NIBRS data are a standard source used to measure criminal offenses by criminal category for LEAs that report into the NIBRS. However, not all LEAs report their data to the NIBRS.[154]

85. Starting with 2011, NIBRS does not include crime counts for some LEAs. Where data are missing in the NIBRS, my staff contacted the LEA directly to obtain crime reports. Where data remain unavailable, I exclude these LEAs from the count for that year, in effect, conservatively, attributing no crimes to that LEA in that year. LEAs with at least one year of data from 2006-2018 are: The City of Huntington, Cabell County Sheriff's Office, Marshall University, Barboursville Village, The Town of Milton, the Cabell State Police, the State Fire Marshall, and the Cabell County Department of Natural Resources.[155]

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[153] The City of Solutions, Huntington WV, p. 76.

[154] The Bureau of Justice Statistics reported that, "In 2012 NIBRS-contributing agencies served approximately 30 percent of the U.S. population and accounted for 28 percent of all crime reported to the UCR [Uniform Crime Reporting] Program." See Bureau of Justice Statistics, "Data Collection: National Incident-Based Reporting System (NIBRS)" (https://www.bjs.gov/index.cfm?ty=dcdetail&iid=301). Some of the larger LEAs in Cabell County did not report crimes to NIBRS during 2011-2018, including the Huntington Police Department and the Cabell County Sheriff.

[155] Specifics on data available for each of the LEAs are contained in Appendix C. Alternate sources are also explained there.

86. Crime counts include drug-related crimes (possession, selling, or distribution of illegal drugs), where the primary criminal activity relates to drugs, and other crimes (arson, battery, vandalism) that occurred due to drugs. For drug-related crimes, I estimate the share of these that are opioid related based on the share of all drug seizures in West Virginia that involved opioids.[156] I then adjust these crime counts by the share of OUD in Cabell County due directly and indirectly to prescription opioids applying the last row of Table 4. For other crimes (*e.g.*, battery), I use findings from research studies to estimate the share of these crimes that are attributable to drugs.[157] I then apply the same adjustment for drug-related crimes to find the number of other crimes attributable to prescription opioids. See Section IV.1 of Appendix C for details on crime counts.

Valuing the Cost of Crimes

87. A commonly used framework in the economic literature on crime classifies costs into direct, indirect, and intangible costs.[158] Direct costs include medical costs, the costs of private crime deterrents (alarms, security), public expenditures on police, court costs associated with investigating and prosecuting criminal activity, and the value of property lost due to criminal activity. Indirect costs of crime include the productivity loss for victims of violent crime and the loss in productivity due to addiction and incarceration for the perpetrator. Finally, intangible costs consist of pain, suffering, and psychological consequences borne by crime victims and the public.

88. Direct costs of crime are often estimated by combining several sources of data, including government data on criminal justice system costs, surveys on medical expenses, and property

[156] I use West Virginia data reported to the National Forensic Laboratory Information System (NFLIS) on the number of drug crimes involving opioids.

[157] The share of criminal activity due to drugs comes from this report: U.S. Department of Justice, National Drug Intelligence Center, "The Economic Impact of Illicit Drug Use on American Society," 2011 (https://www.justice.gov/archive/ndic/pubs44/44731/44731p.pdf).

[158] Two literature reviews are: N. Wickramasekera, *et al.*, "Cost of Crime: A Systematic Review," *Journal of Criminal Justice*, 43(3), 2015, pp. 218-228 and K.E. McCollister, M.T. French and H. Fang, "The Cost of Crime to Society: New Crime-Specific Estimates for Policy and Program Evaluation," *Drug and Alcohol Dependence*, 108(1-2), 2010, pp. 98-109.

loss associated with crime.[159] The main component of the indirect costs of crime is productivity loss by both the victims and the perpetrators. Crimes that result in injury or hospitalization lead to a reduction in victim productivity. The opportunity cost to criminals of engaging in productive activities is also included in the indirect cost of crime.[160] Finally, intangible costs include the emotional and psychological consequences of criminal activity imposed on victims and the public. The "jury-compensation approach" uses monetary amounts awarded by juries in injury cases, net of medical costs and lost wages, to estimate intangible costs to victims.[161] A second method for estimating intangible costs, the contingent valuation approach, uses surveys to estimate respondents' willingness-to-pay for reductions in hypothetical risk of pain, suffering or various types of crimes. See Appendix C, Section IV.2 for further descriptions regarding crime valuation.

89. Another perspective on costs comes from considering the value of public services police could have provided had they not been diverted into opioid-related crimes. The surge in opioid-related crime consumed much of the Huntington Police Department officers' time and resources. According to Captain Dial, "the detectives have had a hard time handling the workload ..."[162] Diversion of police resources to opioid-related crime means less resources available for other law enforcement activities, for example, increasing wait times after a call and less police time available for investigation. As Chief Ciccarelli explained in *The Herald Dispatch*, "We maintained our staffing where it's at to ensure we can make these [overdose] calls, but to do that, other areas have had to suffer." The suffering referred to by the Chief is experienced by the residents of the Cabell Huntington Community. Cabell County Sheriff Charles Zerkle confirms

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[159] See D.A. Anderson, "The Cost of Crime," *Foundations and Trends® in Microeconomics*, July 3. 2011, pp. 209-265, chapter 4, for a discussion and a representative example of the data-aggregation methods used in crime costing studies.

[160] These costs are often calculated by multiplying the minimum wage by the amount of person-years spent by criminals in incarceration. This assumes incarcerated individuals would work full time at a low-paying job if not incarcerated. This measure is likely an underestimation of this form of crime cost because it omits the opportunity cost of crime that does not result in incarceration. See McCollister *op. cit*.

[161] This methodology was developed in M.A. Cohen, "Pain, Suffering, And Jury Awards: A Study of the Cost of Crime to Victims," *Law & Society Review*, 22(3), 1988, pp. 537-555.

[162] J. Qualls, and C. Hessler, *op. cit.*

his office's inability to keep up with the rash of opioid-related crime: "… We were overwhelmed and we lacked resources, and we continued to lack resources to do our job."[163]

90. Sheriff Zerkle was explicit about the cost of devoting police resources to opioid-related problems in schools. In his deposition he states: "… I have five [deputies] that are assigned to schools. They're school resource officers. I took some flack over that a little bit, that I pulled that many people. I have 12 percent of my workforce in the schools. But what's happened during this timeline, our children, they've lost their families, they've lost their mothers and fathers. Now the grandparents are trying to raise them. And disruption in the school and stuff, I thought it was a good investment in our kids and our future to put those five deputies in the schools."[164]

91. Table 8 presents dollar estimates of the costs of crime across all types of offenses for the Cabell Huntington Community. These figures include direct, indirect, and intangible costs as described above. In total, I estimate that crimes due to sales and distribution of prescription opioid from 2006-2018 led to excess costs of over $77.4 million in the Community.

[163] Deposition of Charles Zerkle, in this matter, June 17, 2020, (hereafter Zerkle Deposition), p. 190.

[164] Zerkle Deposition, pp. 71-72.

Table 8
Crime and Valuation of Crime Attributed to
Prescription Opioid Sales and Distribution
Cabell Huntington Community, 2006-2018

		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
[1]	Crime events attributable to prescription opioids	482.1	447.4	543.4	842.9	657.6	545.6	734.1	700.2	977.8	860.7	917.7	749.8	730.3	9,189.8
[2]	Costs for crimes attributable to prescription opioids ($millions)	$3.7	$3.7	$4.8	$7.0	$5.3	$4.4	$5.7	$5.7	$7.3	$6.5	$8.3	$8.1	$7.0	$77.4

Sources: Appendix C, Tables C.IV.1 - C.IV.4.

E. Prescription Opioid-Related Crime and Property Values

Overview

92. One pernicious and impossible-to-miss harm from the opioid epidemic is neighborhood blight, the degradation of neighborhoods contaminated by drug sellers, drug users, and crime. The association between crime, empty homes, and neighborhood decline is widely documented.[165] Homes and neighborhoods in the Cabell Huntington Community have been severely adversely affected by the opioid epidemic, with hundreds of homes demolished due to abandonment, crime, and uninhabitability. From a December 2019 report in the *West Virginia Metro News*:

> "[City of Huntington Demolitions Specialist Crystal] Perry said Huntington Mayor Steve Williams and others began looking at the abandoned house issue a few years ago with the rise of the opioid epidemic. She said there were originally about 500 structures identified. The list of remaining structures is now down to about 130."[166]

93. For many households in Cabell, a home is their primary form of wealth. The median net wealth of American households, as measured by net worth, was $94,670 in 2016, with 34.5% of

[165] See, for example, I.G. Ellen, J. Lacoe, and C.A. Sharygin, "Do Foreclosures Cause Crime?" *Journal of Urban Economics*, 74, 2013, pp. 59-70; L. Cui, and R. Walsh, "Foreclosure, Vacancy and Crime," *Journal of Urban Economics*, 87, 2015, pp. 72-84; and J. J. Roth, "Empty Homes and Acquisitive Crime: Does Vacancy Type Matter?" *American Journal of Criminal Justice*, 44(5), 2019, pp. 770-787.

[166] J. Jenkins. "Huntington House Demo Number Climbs to 100." *WV MetroNews*, December 23, 2019 (wvmetronews.com/2019/12/23/huntington-house-demo-number-climbs-to-100/).

that composed of home equity.[167] Home ownership is an especially important financial asset for individuals at the lower end of the income distribution.[168] Crime-caused loss in home value can impose substantial harm on all residents of affected communities. A safe, comfortable home is, of course, more than a holding in a financial portfolio.

94. The residential housing market in Cabell County shows signs of being depressed due to the opioid epidemic. The addition of new housing stock in Cabell County declined dramatically starting in 2013, going against state and national trends.[169] The average listing price of Cabell County housing declined significantly from 2017-2019.[170] During 2006-2018, West Virginia's house pricing index increased steadily whereas Cabell County's remained relatively flat.[171] The population of Cabell County has fallen since 2013.[172] A recent news article, however, reports a rebound in the Cabell housing market.[173]

95. The opioid epidemic degrades neighborhoods along many dimensions. Risk of crime, loss of safe public space, loss of connection with neighbors and other harms interfere with residents' ability to appreciate where they live. Degradation lowers home property values and

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[167] J. Eggleston and R. Munk, "Net Worth of Households: 2016," *US Census Bureau Report P70BR-166*, 2019.

[168] "Houses are *the* asset of the bottom 90%, making residential real estate the most egalitarian asset ... The bottom 90% hold about half of all housing wealth …" in M. Kuhn, M. Schularick, and U. Steins, "Income and Wealth Inequality in America, 1949-2016," Opportunity & Inclusive Growth Institute, Federal Reserve Bank of Minneapolis, Institute Working Paper No. 9, June 2018, p. 35.

[169] U.S. Census Bureau, New Private Housing Structures Authorized by Building Permits for Cabell County, WV [BPPRIV054011], West Virginia [WVBPPRIV], and nationwide [PEMIT] retrieved from FRED, Federal Reserve Bank of St. Louis (https://fred.stlouisfed.org/series/BPPRIV054011, April 21, 2020. Graph available here: https://fred.stlouisfed.org/graph/?g=qMe1).

[170] Realtor.com, Housing Inventory: Average Listing Price in Cabell County, WV [AVELISPRI54011], retrieved from FRED, Federal Reserve Bank of St. Louis (https://fred.stlouisfed.org/series/AVELISPRI54011, April 21, 2020).

[171] U.S. Federal Housing Finance Agency, All-Transactions House Price Index for Cabell County, WV [ATNHPIUS54011A], (https://fred.stlouisfed.org/series/ATNHPIUS54011A, June 24, 2020) and West Virginia [WVSTHPI], retrieved from FRED, Federal Reserve Bank of St. Louis, (https://fred.stlouisfed.org/series/WVSTHPI, May 26, 2020). Realtor.com, Housing Inventory: Average Listing Price in Cabell County, WV [AVELISPRI54011], retrieved from FRED, Federal Reserve Bank of St. Louis (https://fred.stlouisfed.org/series/AVELISPRI54011, July 2, 2020).

[172] U.S. Census Bureau, Resident Population in Cabell County, WV [WVCABE1POP], retrieved from FRED, Federal Reserve Bank of St. Louis (https://fred.stlouisfed.org/series/WVCABE1POP, April 21, 2020).

[173] "I. Johnson: Progress is Happening in Cabell County, and the Assessor's Office," *The Herald Dispatch*, March 20, 2020 (https://www.herald-dispatch.com/news/irv-johnson-progress-is-happening-in-cabell-county-and-the-assessors-office/article_632ab6e0-4fbb-5cd5-9361-a3ed46d2fab9.html).

lowers residents' valuation of parks, public transportation, schools, and other local public services.[174]

96. In this section, I address the question, "How much higher would property values in the Cabell Huntington Community be absent the crimes due to prescription opioids?" The economic model I apply to answer this question can be depicted as follows:

$$Prescription\ Opioids \rightarrow Elevated\ Crime\ Rates \rightarrow Decrease\ in\ Property\ Values$$

97. The first causal link, between prescriptions and crime, has already been covered in Section III.D. Overall, I calculate that prescription opioids were responsible for 7.2% of total crimes in the Cabell Huntington Community over the period 2006 to 2018.[175] The second causal arrow, between crime and property values is covered in Section IV.3 of Appendix C. With the magnitude of this second section quantified, I can quantify the decrease in property values that has resulted from prescription opioid-related crimes. This property value lost due to crime associated with the sales and distribution of prescription opioids is an economic harm caused by prescription opioids.

98. The value of residential property in Cabell County in 2019 was $5.13 billion. Eliminating the crime associated with the sales and distribution of prescription opioids would increase this value by 1.8%, or $92.3 million. See Section IV.3 of Appendix C for details of these calculations.

[174] Lower crime rates "unlock" the value of public parks in Chicago, New York and Philadelphia according to a study by Albouy and colleagues. Parks have a positive effect on local housing prices in low-crime areas but this positive effect turns negative in higher crime areas. D. Albouy, P. Christensen, I. Sarmiento-Barbieri, "Unlocking Amenities: Estimating Public-Good Complementarity," National Bureau of Economic Research, Working Paper 25107, revised July 2019. The relation between the amenity value of public parks and crime was also studied by Troy and Grove in Baltimore with the same result. High crime turns a public good into a public bad. A. Troy. and J.M. Grove, "Property Values, Parks, and Crime: A hedonic analysis in Baltimore, MD," *Landscape and Urban Planning*, 87(3), 2008, pp. 233-245.

[175] The total number of crimes in Cabell County during 2006-2018 is 128,376 (see Appendix C for source). Table 8 of my Report shows that 9,189 crimes were attributable to prescription opioids. The ratio of these numbers yields this estimate.

F. Child Maltreatment

Overview

99. Substance abuse, including opioid abuse, is a major cause of child maltreatment.[176] According to the U.S. Department of Health and Human Services, in fiscal year 2018, approximately 678,000 children were subject to abuse and neglect in the U.S. This amounts to about 9.2 victims per 1,000 children nationwide.[177] In West Virginia, the victimization rate in 2018 was 19.1 per 1,000 children.[178] Drug abuse in a household is a major risk factor associated with child maltreatment. Nationally, 30.7% of 2018 victims lived in households with caregivers with drug abuse risk factors.[179] The analogous figure in West Virginia is 57.1%[180]

100. Like other harms, my valuation of the economic harm from child maltreatment is the product of the number of victims where prescription opioids were involved multiplied by the costs associated with this maltreatment. Although maltreated children face a host of negative consequences, for the purposes of my valuation, due to data limitations, I focus on lost earnings in adulthood due to lower educational attainment, plus special educational services provided to maltreated children.

101. In an aggressive effort to combat harms to children from the opioid epidemic, Cabell Huntington Community leaders have created programs for vulnerable women and children. One such effort is Project Hope. Initially administered by the Huntington City Mission, Project Hope expanded the number of transitional housing units available to women in recovery and their children.[181] These homes come with 24-hour care and clinical services including group therapy

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[176] See Children's Bureau, Office of the Administration for Children and Families, U.S. Department of Health & Human Services (HHS), "Child Maltreatment 2018," 2019, (https://www.acf.hhs.gov/sites/default/files/cb/cm2018.pdf); O. Mowbray, *et al*., "Longitudinal Trends in Substance Use and Mental Health Service Needs in Child Welfare," *Children and Youth Services Review*, 73, February 2017, pp. 1-8.

[177] HHS (2019), *op. cit.*, p. 21.

[178] HHS (2019), *op. cit.*, p. 30.

[179] Drug abuse is defined as "…the compulsive use of drugs that is not of a temporary nature." HHS (2019), *op. cit.*, p. 21, 43.

[180] HHS (2019), *op. cit.*, p. 43.

[181] The City of Solutions, Huntington WV, p. 38.

and MOUD. Moreover, Project Hope also provides fitness classes, GED training, peer coaching, and job training events.

102. Healthy Connections is another such effort.[182] This program aims to reintegrate recovering participants into society, via the use of navigators – case workers with small caseloads who specialize in issues faced by women and children suffering from the consequences of substance abuse. Healthy Connections navigators and coaches start work with participants as early as possible, design specialized recovery plans tailored for the unique circumstances faced by each participant, and provide guidance through the full re-entry process. In addition, navigators integrate other members of the family, particularly grandparents and fathers of the children, in order to better care for these at-risk children.

Count of Victims of Maltreatment

103. I estimate the number of children maltreated due to the sales and distribution of prescription opioids in the Cabell Huntington Community in five steps. First, I obtain three data series from the HHS's Administration for Children and Families (ACF): the number of maltreatment victims that are first-time, unique, and unique with a drug abuse risk factor in West Virginia.[183] Second, I take the ratio of first-time to unique victims, and apply that to the number of unique maltreatment victims with a drug abuse risk factor, in order to estimate the number of first-time victims with a drug abuse risk factor. Third, I adjust these state-wide counts by the number of children in Cabell County to obtain County-level numbers. Fourth, to estimate the share of drug abuse-related maltreatment victims attributable to opioids, I multiply the number of drug abuse-related maltreatment victims by the share of drug seizures that involved opioids, as I did in section III.D. above. Finally, I multiply this count by the opioid morbidity attributable to

[182] The City of Solutions, Huntington WV, p. 45.

[183] Administration for Children and Families (https://www.acf.hhs.gov) is a division in the department of Health and Human Services which collects detailed annual information from states on child maltreatment and produces yearly reports on state level incidence of maltreatment, overall and broken out by category, as well as information on characteristics of victims, number of fatalities, services to prevent maltreatment among other metrics. These data are an important source of information for reports to congress and federal government activities. The statistics on child maltreatment are derived from data collected by child protective agencies through the National Child Abuse and Neglect Data system (NCANDS). See Appendix C for the estimation of these counts for 2006-2009, 2013 and 2015 when data is unavailable. Appendix C also has information on the use of first-time maltreat victim counts to avoid double counting over the period.

prescription opioids from the bottom row of Table 4.[184] This gives me an estimate of the number of maltreated children in West Virginia due to prescription opioids.

Valuing the Cost of Maltreatment

104. The research literature establishes that child maltreatment (abuse or neglect) devastates a child, lowering educational attainment;[185] reducing cognitive development;[186] increasing the need for special education services;[187] lowering employment and earnings;[188] and causing higher rates of preventable deaths,[189] obesity,[190] depression,[191] substance abuse,[192] and PTSD.[193]

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[184] Note that for 2006, I use unique maltreatment victim counts, and form 2007-2018, I use first-time victims.

[185] R. Gilbert, *et al*., "Burden and consequences of child maltreatment in high-income countries," *The Lancet,* 373, 2009, pp. 68-81; J. Currie and C.S. Widom, "Long-Term Consequences of Child Abuse and Neglect on Adult Economic Well-Being," *Child Maltreatment*, 15(2), 2010, pp. 111-120; J.P. Mersky and J. Topitzes, "Comparing Early Adult Outcomes of Maltreated And Non-Maltreated Children: A Prospective Longitudinal Investigation," *Children and Youth Services Review*, 32(8), 2010, pp. 1086-1096; J.J. Doyle and A. Aizer, "Economics of Child Protection: Maltreatment, Foster Care, and Intimate Partner Violence," *Annual Review of Economics*, 10, 2018, pp. 87-108; A. Bald, E. Chyn, J.S. Hastings, and M. Machelett, "The Causal Impact of Removing Children from Abusive and Neglectful Homes," NBER Working Paper 25419, January 2019.

[186] K.L. Hildyard and D.A. Wolfe, "Child Neglect: Developmental Issues and Outcomes," *Child Abuse & Neglect*, 26, 2002, pp. 679-695; C.M. Perez and C.S. Widom, "Childhood Victimization and Long-Term Intellectual and Academic Outcomes," *Child Abuse & Neglect*, 18(8), 1994, pp. 617-633; J. Currie & C.S. Widom, *op. cit.*

[187] M. Jonson-Reid, *et al.*, "A Prospective Analysis of the Relationship Between Reported Child Maltreatment and Special Education Eligibility Among Poor Children," *Child Maltreatment*, 9(4), 2004, pp. 382-394; R.J. Gelles and S. Perlman, "Estimated Annual Cost of Child Abuse and Neglect," Prevent Child Abuse America; April 2012 (https://preventchildabuse.org/wp-content/uploads/2016/02/PCA_COM2012-1.pdf); R. Gilbert, *et al., op. cit.*

[188] R.J. Gelles & S. Perlman, *op. cit.;* R. Gilbert, *et al., op. cit.;* J. Currie & C.S. Wido, *op. cit.;* J.P. Mersky and J. Topitzes, *op. cit.*

[189] A. Hjern, B. Vinnerljung, and F. Lindblad, "Avoidable Mortality Among Child Welfare Recipients and Intercountry Adoptees: a National Cohort Study," *Journal of Epidemiology & Community Health,* 58(5), 2004, pp. 412-417.

[190] L.M. Berger and J. Waldfogel, "Economic Determinants and Consequences of Child Maltreatment," OECD Social, Employment and Migration, Working Paper No. 111, April 2011, OECD Publishing, Paris (http://dx.doi.org/10.1787/5kgf09zj7h9t-en); R. Gilbert, *et al., op. cit.*

[191] L.M. Berger and J. Waldfogel, *op. cit.;* R. Gilbert, *et al., op. cit.;* A. Bald, E. Chyn, J.S. Hastings, and M. Machelett, *op. cit.;* J.P. Mersky and J. Topitzes, *op. cit.*; C.S. Widom, K. DuMont, and S.J. Czaja, "A Prospective Investigation of Major Depressive Disorder and Comorbidity in Abused and Neglected Children Grown Up," *Archives of General Psychiatry*, 64(1), 2007, pp. 49-56.

[192] L.M. Berger and J. Waldfogel, *op. cit.*; R. Gilbert, *et al., op. cit.*; J.P. Mersky and J. Topitzes, *op. cit.*; C.S. Widom, K. DuMont, and S.J. Czaja, *op. cit.*

[193] L.M. Berger and J. Waldfogel, *op. cit.*; R. Gilbert, *et al., op. cit.*; C.S. Widom, K. DuMont, and S.J. Czaja, *op. cit.*; C.S. Widom, "Posttraumatic Stress Disorder in Abused and Neglected Children Grown Up," *American Journal of Psychiatry,* 156(8), 1999, pp. 1223-1229.

Furthermore, maltreatment elevates rates of juvenile delinquency[194] and crime.[195] These negative effects of maltreatment are costly. For reasons of data availability, I confine my estimates to harms from two categories: lost earnings and special education costs. For each of these two outcomes, I determine the estimated incremental effect of maltreatment on the outcome.[196]

105. Table 9 reports the dollar estimates of the cost of child maltreatment in Cabell County. I estimate that the social costs of cases of maltreatment attributable to opioid prescription sales and distribution between 2006-2018 in Cabell County was over $57.9 million.

Table 9
Child Maltreatment Victims and Costs Attributed to Prescription Opioid Sales and Distribution
Cabell County, 2006-2018

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
Maltreatment victims attribuatble to prescription opioids	3	2	2	4	4	4	5	7	6	6	55	53	51	201
Costs for child maltreatment attributable to prescription opioids ($ millions)	$0.81	$0.50	$0.68	$1.05	$1.03	$1.21	$1.43	$1.91	$1.76	$1.87	$15.78	$15.19	$14.71	$57.9

Sources: Appendix C, Tables C,V.1 and C.V.2.

[194] C.S. Widom, "The Cycle of Violence," *Science*, 244(4901), 1989, pp. 160-166; R.J. Gelles & S. Perlman, *op. cit.*; R. Gilbert, *et al.*, *op. cit.*; M.G. Maxfield and C.S. Widom, "The Cycle of Violence: Revisited 6 Years Later," *Archives of Pediatrics & Adolescent Medicine*, 150(4), 1996, pp. 390-395; C.S. Widom and M.G. Maxfield, "An Update on the 'Cycle of Violence.' Research in Brief," U.S. Department of Justice, February 2001 (https://files.eric.ed.gov/fulltext/ED451313.pdf).

[195] J. Currie and E. Tekin, "Does child abuse cause crime?" NBER Working Paper 12171, April 2006; Doyle and Aizer, *op. cit.*; R.J. Gelles & S. Perlman, *op. cit.*; R. Gilbert, *et al.*, *op. cit.*; Widom, *op. cit.*; J. Currie and E. Tekin, "Understanding the cycle: Childhood Maltreatment and Future Crime," *Journal of Human Resources*, 47(2), 2012, pp. 509-549; J.P. Mersky and J. Topitzes, *op. cit.*; M.G. Maxfield and C.S. Widom, *op. cit*; C.S. Widom and M.G. Maxfield, *op. cit.*

[196] See Appendix C.

IV. The Economic Costs Imposed by Sales and Distribution of Prescription Opioid Products are of Sufficient Magnitude to Constitute a Public Nuisance to the Cabell Huntington Community

A. Summary of Costs Imposed

106. Table 1, repeated here from the Introduction, summarizes the costs associated with categories of harms studied above from 2006-2018. Over these thirteen years, the costs attributable to the sales and distribution of prescription opioids in the Cabell Huntington Community totaled over $4.17 billion dollars, implying a cost of over $43 thousand per Cabell Huntington Community resident.

107. I regard my estimates of the costs imposed by the sales and distribution of prescription opioids to be conservative for a number of reasons. First, due to limitations on data availability, my calculations do not include the years 2019 and 2020. If I use the cost for 2018 as an estimate of the costs for each of 2019 and 2020, my estimates increase by $1.7 billion. Further, my calculations for each of the harms I address are based upon a series of conservative assumptions, some of which are noted in Table 10.

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Table 1
Monetary Value of the Net Costs Attributed to the Sales and Distribution of Prescription Opioids in the Cabell Huntington Community 2006-2018

Harms Due to Sales & Distribution of Prescription Opioids	Valuation ($millions)
Excess deaths	$3,437.8
Excess morbidity	$501.3
Excess neonatal abstinence syndrome	$2.6
Excess crimes	$77.4
Excess property value loss	$92.3
Excess child maltreatment	$57.9
Total	**$4,169.2**

Sources: Tables 3, 5, 7, 8, 9, and Section III.E of this Report.

Table 10
Conservative Assumptions Applied in Estimating Costs in this Report

Harm	Conservative Assumptions
Mortality	• Does not include damage to community fabric, financial dependents of those who died, compassion fatigue among first responders • VSL valuation is U-shaped, implying higher valuation for working-age adults. Opioid deaths are largely working-age adults • Does not include portion of Huntington in Wayne County
Morbidity	• Only accounts for OUD treatment related health care expenditures paid by third parties • Undercounts costs of comorbidities such as Hepatitis, HIV, and infectious endocarditis • Does not include community efforts and centers specifically launched to combat the effects of OUD • Does not quantify the net negative effects on labor-force participation and productivity • Does not include portion of Huntington in Wayne County
NAS	• Excludes community efforts to treat NAS cases, such as Lily's Place and Project Hope • Does not include the adulthood costs from lower educational outcomes due to NAS, such as upward mobility, income, and others • Does not include portion of Huntington in Wayne County • Does not include case counts beyond 2015
Crime	• Crime counts of criminal activity are lower than actual due to LEAs not reporting • Excludes stress to first responders and others in the community from increased criminal activity
Property Values	• Costs were assessed on residential property only • Does not include portion of Huntington in Wayne County
Maltreatment	• Excludes valuation of other maltreatment consequences: juvenile delinquency, preventable death, lowered mental health, increase in substance abuse rates, and PTSD • Does not include portion of Huntington in Wayne County

B. Costs Imposed Were of Sufficient Magnitude to Constitute a Public Nuisance

108. Since from the year I have been asked to monetize harms, 2006, and likely earlier, the Community has been awash in prescription opioids. Shipment data produced in related litigation shows that between 2006 and 2014, manufacturers and distributors shipped hydrocodone and oxycodone opioids to the State of West Virginia sufficient to give 611 pills to every man, woman and child in the state.[197] The situation in Cabell County was even more dire. Dr. McCann, in his report, quantifies the volume of morphine milligram equivalents (MMEs) shipped into Cabell County.[198] He reports that over 3.2 billion MMEs or approximately 128 million dosage units were shipped into Cabell County from 2006-2014, equivalent to over 1,300 doses for each Cabell County resident.[199]

109. County and city officials attest to the ongoing public nuisance in the Community caused by the opioid epidemic. For example, Beth Thompson, Administrator for the Cabell County Commission, in her deposition,[200] stated her view:

> "Q. You testified earlier that you knew – why do you believe it's a public nuisance now?
>
> A. Because of the health and safety of our community has been compromised. …
>
> Q. Are there any indicators to you that would signify that the nuisance is over?
>
> A. Maybe when we don't have to have Lily's Place where people sit and rock babies that won't quit crying because they're, you know, addicted to drugs when they're born. Maybe when I can look out my window at work and not see somebody having an overdose on the lawn of the courthouse. Or going by our vehicles and stabbing each other and we have to have security officers walking us to the cars in the evenings and to the courthouse in the mornings. Stealing people's -- kids' bicycles out of their yards. You know, maybe when there's an end to all that, maybe it's over."

110. Fire Chief Rader explained some of the community-wide and ongoing harms:

> "…you have a whole generation of grandparents raising their grandchildren because adults are behind bars or have died opioid-related deaths… You have people incarcerated who…may have a felony hanging over their head, which makes it very difficult for them to find employment….You have first responders that will probably never be able to recover

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[197] Complaint, ¶ 4.

[198] Expert Report of Craig J. McCann, Ph.D., CFA, in this matter, August 3, 2020, Table 15, p. 79.

[199] Based on the 2018 Cabell Huntington Community population of 96,619.

[200] Deposition of Beth Thompson, in this matter, July 7, 2020, pp. 248-249 (counsel objections omitted).

> from this….How do you support the children that watch their parents overdose? They're being put into the foster care system. "[201]

Later, when asked to describe the opioid epidemic:

> Q. And Chief Rader, if you could describe the opioid epidemic in Huntington with one word, what would that be?
>
> A. It's horrific.[202]

107. In 2015, the Mayor of Huntington, Steve Williams, conveyed the magnitude of the harms: "The epidemic of addiction is now so pervasive that our standard of living, our way of life and our children's future is at stake."[203] In deposition, when asked if prescribing opioids is a public nuisance, Mayor Williams responded "If it leads – yes, if it leads to public health problems and public safety problems, as it has."[204] The Mayor gave direct and unambiguous responses to questions related to prescription opioids as a public nuisance:

> Q. Does the opioid epidemic interfere with the public health in the City of Huntington?
>
> A. Yes.
>
> Q. Does the opioid epidemic interfere with the public safety in the City of Huntington?
>
> A. Yes.
>
> Q. Mayor, based on your experience living in the City of Huntington and serving as the mayor of the City of Huntington, do you believe there presently exists a hazard to the public health and safety arising out of a prescription opioid epidemic?
>
> A. Yes.[205]

111. After review of the evidence on the harms caused by the sales and distribution of prescription opioids to the Cabell Huntington Community, including the testimony of local officials, I am aware that the dry economic language of "costs and benefits" is inadequate to convey the full magnitude of the destruction wrought by prescription opioids on the Community. The economic concept of "costs" is useful to quantify the harms with a common denominator of

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[201] Rader Deposition, pp. 197-199

[202] Rader Deposition, p. 265.

[203] Mayor Steve Williams, City of Huntington, Letter to the residents of Huntington and the Tri-State Region, in: City of Huntington, Mayor's Office of Drug Control Policy, "2017 Strategic Plan," May 2017, p. ii.

[204] Williams Deposition, p. 50.

[205] *Ibid.*, p. 300.

dollars, enabling an economist to add them up using one metric. But actual harms take place in real-life terms, and in many forms: babies born addicted to opioids facing a lifetime of disability and disadvantage, the risk of opioid-related crimes degrading home values because of the lower quality of life caused by crime, death and disease of sufficient magnitude to touch nearly every family in the community.

112. Ongoing harms of more than $4 billion imposed on a small community over 13 years establish that the harms from prescription opioids are of sufficient magnitude to constitute a public nuisance. The population of the Cabell Huntington Community was 96,619 in 2018.[206] The costs reported in Table 1 amounted, over the period covered in my Report, to approximately $43 thousand per person in the Community. These costs are net of any economic benefits from workforce participation.

113. The position of the Cabell Huntington Community relative to the national opioid crisis yields another perspective. As a rule of thumb (see Figures 2 and 5 above), opioid-related harms in the Cabell Huntington Community are an *order of magnitude greater* than nationwide. Looked at another way, by some metrics, West Virginia has been the state hardest hit by prescription opioids, and within West Virginia, Cabell County has been the 3rd hardest-hit county.[207] Cabell has been referred to as "ground zero" of the opioid crisis.[208] If the sales and distribution of prescription opioids qualify as a public nuisance anywhere, they qualify in the Cabell Huntington Community.

114. Based on the cost analysis in Section III, I conclude that the harms to the Community caused by the sales and distribution of prescription opioids are of sufficient magnitude to constitute a public nuisance. My economic analysis establishes that the sales and distribution of prescription opioids has interfered with public health, safety, peace, and comfort of residents of the Cabell Huntington Community, with economically large, continuing, and long-lasting effects.

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[206] U.S. Census, County Population by Characteristics, 2010-2019. Estimate for 2018 (https://www.census.gov/data/tables/time-series/demo/popest/2010s-counties-detail.html).

[207] See, for example, the NAS rate in Cabell County, Figure 7, the number of opioid shipments compared to West Virginia and nationwide.

[208] C. Babcock, N. Rockich-Winston, and C. Booth, "Bringing Naloxone to Ground Zero: Huntington, West Virginia," *Journal of the American Pharmacists* Association, 57.2, 2017, pp. S9-S10.

My Report quantifies in dollar terms the negative effects of death, disease, children born addicted, crime, loss of property values, and child maltreatment.

Pursuant to 28 U.S.C. S 1746, I declare under penalty of perjury that the foregoing is true and correct.

_____

Thomas McGuire

August 3, 2020

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA

* *

THE CITY OF HUNTINGTON,

Plaintiff,

vs. CIVIL ACTION
NO. 3:17-01362
AMERISOURCEBERGEN DRUG
CORPORATION, et al.,
Defendants.

CABELL COUNTY COMMISSION,
Plaintiff,
vs. CIVIL ACTION
NO. 3:17-01665
AMERISOURCEBERGEN DRUG
CORPORATION, et al.,

Defendants.

* *

Videotaped and videoconference deposition of THOMAS MCGUIRE taken by the Defendants under the Federal Rules of Civil Procedure in the above-entitled action, pursuant to notice, before Teresa S. Evans, a Registered Merit Reporter, all parties located remotely, on the 9th day of September, 2020.

APPEARANCES:

APPEARING FOR THE PLAINTIFFS:

Michael Pendell, Esquire
David D. Burnett, Esquire
Anne McGinness Kearse, Esquire
John Hurst, Esquire
MOTLEY RICE
28 Bridgeside Boulevard
Mt. Pleasant, SC 29464

David Ko, Esquire
KELLER ROHRBACK LLP
1201 Third Avenue, Suite 3200
Seattle, WA 98101

APPEARING FOR THE DEFENDANT CARDINAL HEALTH:

J. Andrew Keyes, Esquire
WILLIAMS & CONNOLLY
725 Twelfth Street, N.W.
Washington, DC 20005
Raymond Franks, Esquire
CAREY, DOUGLAS, KESSLER & RUBY
901 Chase Tower
707 Virginia Street, East
Charleston, WV 25323

APPEARING FOR THE DEFENDANT AMERISOURCEBERGEN:

Cliff Breese, Esquire (morning)
Alyssa Conn, Esquire (afternoon)
REED SMITH
Three Logan Square
1717 Arch Street, Suite 3100
Philadelphia, PA, 19103

APPEARANCES (Contd.):

ALSO PRESENT:

Adam Hager, Videographer
Justin Taylor, Esquire (via Zoom)

EXAMINATION INDEX

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A. You mean is sales different than distribution?
Q. Yes. As you use the term in your report.
A. Well, they're -- they, I think, refer to somewhat different things as part of the process by which prescription opioids move from the manufacturer to the consumer.
Q. Okay. I'm just trying to understand whether when you use the phrase "sales and distribution," that's referring to one thing or it's referring to two things.
A. Oh.
Q. And I believe what you've said is it means two different things. One is distribution means the shipment of the goods from manufacturer to retail; and the sales is when someone at the retail level is -- is buying or selling something.
Is that a fair encapsulation of how you mean the terms?
MR. PENDELL: Objection.
A. Well, I -- it's -- in response to your question, I was answering -- attempting to give a kind of definition of what distribution is and what sales are. It's one, you know, kind of process in

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a way in which the drugs move from the manufacturer to the retail.
I'm not sure what you're getting at in your question.
Q. Okay. When you refer to "sales and distribution of prescription opioids," you're referring to distribution as going from manufacturer to retail. Is that accurate?
MR. PENDELL: Object to the form.
A. You know, I haven't thought of this as a kind of a narrow issue. I'm pausing to think about your question.
So I would say, you know, sales and distribution - you know, unless I'm missing something subtle here that I just don't see - yes, refers to the movement of opioids from, you know, the manufacturer ultimately to -- ultimately to retail, and from there, being sold to consumers.
Q. And in this report, you are quantifying the harms imposed by all sales and distribution of prescription opioids from 2006 through 2018. Correct?
A. Well, yes. These are net harms. But yes. Other than that, I agree with your statement.

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Q. And so in quantifying the harms resulting from the sale or distribution of prescription opioids, you didn't exclude any prescription opioid sales or distributions during that time period, 2006 to 2018. Correct?
A. Didn't exclude.
MR. PENDELL: I'm just going to object to the form of that question.
But you can answer, Professor.
A. Well, I considered, in total, the net harms or net costs associated with the sale and distribution of prescription opioids. I didn't think of myself as excluding anything.
Q. Right. But I'm trying to say, was there some category of prescription opioids that were sold and distributed that you excluded from your quantification of the harms?
A. No, I don't think so. I think I included everything.
Q. Did you separate out the harms that were imposed by the sales and distribution of prescription opioids from 2006 through 2018 by actors other than the defendants in this case?
A. I'll get to that, but I want to be clear.

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You -- I don't object to the word "harms," but costs would be a more accurate phrase in what I came up with.
MR. PENDELL: I'll -- I'll object to the word.
Go ahead.
A. In response to your question, my assignment was not to allocate responsibility for the costs across, you know, different parties in the case.
Q. Okay. So did you separate out the economic harms that were imposed by the sales and distribution of prescription opioids from 2006 through 2018 by actors other than the defendants in this case?
MR. PENDELL: Objection to form.
A. My -- my role was to estimate the total, and I understand that not to have involved separating out the contribution of different actors.
Q. During the time period covered by your report - 2006 through 2018 - who did you understand to be the whole -- wholesale distributors of prescription opioids in Cabell County, West Virginia?

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A. My understanding goes -- would be based on the defendants in this case, and that would be the basis of my understanding of who was doing the distributing.

Q. Can you list them then? Who you believe were wholesale distributors of prescription opioids in Cabell County, West Virginia between 2006 and 2018?

MR. PENDELL: Objection.

A. Yeah, I don't know the market shares - if I could use that term - in Cabell County of the role of different distributors. So I can't answer it from that perspective.

The perspective I can answer it from is who are listed defendants in the case.

Q. Okay. Were there sellers of prescription opioids in Cabell County, West Virginia between 2006 and 2018 who did not get the prescription opioids they sold from wholesale distributors?

MR. PENDELL: Object to the form.

A. I'm not sure.

Q. Okay. Are you able to identify whether there were any sellers of prescription opioids in Cabell County, West Virginia who did not get

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prescription opioids they sold from wholesale distributors?

MR. PENDELL: Objection.

A. No, I'm not able to identify any seller of that category.

Q. Okay. Is it accurate to say that you quantified the economic harms imposed by the sale and distribution of all prescription opioids from 2006 through 2018 and not just the economic harms of selling and distributing prescription opioids above a certain threshold amount?

MR. PENDELL: Objection to form.

A. Yes. My understanding of my assignment would be to -- to, you know, account the net costs of all prescription opioids, you know, without attempting to segment them into various categories.

Q. So did you -- did you segment the economic harms imposed by the sale and distribution of prescription -- prescription opioids between an appropriate amount of sales and distribution versus an inappropriate amount of sale and distribution?

MR. PENDELL: Objection to form.

A. My task was to consider the total, and issues with respect to clinical appropriateness

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were not within my purview in this report.

Those inputs came from elsewhere.

Q. Okay. So again, you quantified what you call the net economic harm imposed by the sale and distribution of all prescription opioids in Cabell County, West Virginia from 2006 through 2018, right?

A. That's very close. I would say, "net cost," though. But yes, it's the net cost over that time period of the sale and distribution of all prescription opioids.

Q. So you think it should say, "net costs" rather than "net economic harms"?

A. I like "net costs" better, yes.

Q. Okay. And then you didn't do anything to further separate out or segment or tease out the economic harms based on an appropriate level of sales and distribution versus an inappropriate level of sales and distribution.

MR. PENDELL: Objection to form.

Q. Right?

A. Well, that's, I think, the same question I got a minute ago, and my answer is the same: That my job was to look at the total net -- the net

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costs of -- of the sale and distribution of all prescription opioids over that time period.

And issues with respect to clinical appropriateness were not part of my assignment.

Q. Okay. Did you separate out or segment out or tease out the net economic harms or costs imposed by an excessive amount of sales and distributions of all prescription opioids versus a reasonable level of sale and distribution of prescription opioids?

MR. PENDELL: Objection.

A. Well, "reasonable" and "excessive" in this context, I think, are clinical terms. At least I understand them to be clinical terms. Issues which were addressed by other plaintiff experts. I used those opinion -- opinions as inputs, but my job was to look at the total and look at the net.

Q. Okay. Without regarding to a dividing line between appropriate and inappropriate.

A. Well, that would have been factored in by the clinical experts.

Q. Okay. Without regard to the dividing line between reasonable and unreasonable.

A. Again, that would have been factored in by

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the clinical experts.
Q. Without regard to the dividing line between a reasonable amount of sale and distribution of opioids versus an excessive amount of sale and distribution of prescription opioids.
A. I also hear that as a question about clinical matters, which the clinical experts would have taken into account and used -- and I would use those inputs in my report.
Q. And do you articulate the dividing line between a tolerable level of sales and distribution of prescription opioids versus an intolerable level?
MR. PENDELL: I'll object.
A. Well, I don't know what "intolerable" means, but I don't think I need to know the answer to that in your question.
That if it's a clinical matter, then, again, it was the clinical side of the expertise in this case that would have made those determinations.
Q. And do you articulate the dividing line between the amount of sale and distribution of prescription opioids that constitutes a nuisance

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versus the level of sale and distribution of prescription opioids that does not constitute a nuisance?
A. You know, I wasn't asked that question. I was asked with respect --
Sorry, there's an insect trying to get on the video.
No, I was asked the question of: In total, did sale and distribution of prescription opioids constitute a public nuisance? Not whether there might have been, you know, some other situation in which they could be divided into those that were and those that were not.
Q. And when you quantify the net economic harms or the net economic costs imposed by the sales and distribution of prescription opioids from 2006 through 2018 in Cabell County, West Virginia, you're quantifying all of those, not the ones that are attributable to conduct of particular actors.
Is that correct?
A. Yes, I think that's correct. My job was to pick up the story at the point of assessing the net costs of the sale and distribution. Why that took place was not part of my assignment.

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Q. So did you take any steps to eliminate from your calculations the economic harms or the costs of prescription opioids that were sold and distributed by the defendants in this case without breaching any duty?
MR. PENDELL: Objection.
A. I think the answer to that is I did not try to segment the sale and distribution of prescription opioids nor the economic costs associated with them according to a categorization of the nature of the sale and distribution.
Q. And are you offering any opinion of what portion of the net economic harms or costs you quantified are due to the sale and distribution of prescription opioids by the defendants in this case?
A. I've got the total in my report, and I -- and so I would say -- I also did not - as part of my assignment - apportion that to particular defendants. Or non-defendants. I just -- I didn't do it.
Q. And did you do any apportionment of the net economic harms or costs that were imposed by the sales and distribution of prescription opioids from

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2006 through 2018 in Cabell County, West Virginia, to the unlawful sale or the unlawful distribution of prescription opioids by the defendants?
MR. PENDELL: Objection.
A. Well, I wouldn't be in a good position to say what is lawful and unlawful, but I think I can answer the question anyway.
My assignment dealt with the total, and I didn't attempt to apportion it into a category of lawful and unlawful, even if I were able to know what that meant in this case.
Q. Did you make any assessment of which sales and distribution of prescription opioids by defendants were the result of filling and shipping a suspicious order?
MR. PENDELL: Objection.
A. My -- again, my emphasis was on the total, and this would be a different way to think about a partition of the shipments and sales, and I didn't partition it in this way either.
Q. Did you make any assessment of which of the prescription opioids that were sold or distributed by defendants in this case were justified by a clinical need?

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MR. PENDELL: Objection.
A. Well, certainly not at the individual level did I attempt to determine whether individual prescriptions were a result of medical need. But again, this is in the clinical realm and was something that was considered by the clinical experts in this case, and they provided helpful input into my report regarding that.
Q. Well, you didn't do it at the individual level; you also didn't do it at the macro level, correct?
A. Well, I wanted to, you know, be clear what I didn't do. And, yes, I didn't do it at the individual level. And also, yes, I relied on clinical inputs for the macro level.
Q. Did you make any assessment of which of the prescription opioids that were sold and distributed by defendants were used for scientifically-acceptable treatment?
MR. PENDELL: Objection.
A. This is a clinical question as I hear it, and my assignment had to do with the total, and issues that have to do with the clinical component of which would be acceptable, which would be

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unacceptable, were dealt with by clinical experts in this case.
Q. Did you make any assessment of which of the prescription opioids that were sold and distributed by defendants in this case were taken by people pursuant to prescriptions written to them by their treating physician?
A. That's another partition of the total that I did not undertake.
Q. Did you make any assessment of which of the prescription opioids that were sold and distributed by defendants in this case were dispensed by pharmacies to patients pursuant to legitimate prescriptions written by licensed physicians?
MR. PENDELL: I'll object.
Go ahead.
A. Well, this is a new -- a different form of partition, which I did not undertake. My assignment had to do with a total.
Q. Did you make any assessment of which of the prescriptions that were sold and distributed by defendants were diverted long after they left the closed distribution system?
MR. PENDELL: Objection.

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A. No, I didn't make a quantification of diversion in this case.
Q. Is the work you did based on the premise that all sales and all distribution of prescription opioids by the defendants in this case was unlawful?
A. No.
Q. Then did you differentiate at all between the economic harms or costs that were imposed by the unlawful sale and distribution of prescription opioids versus the lawful sale and distribution of prescription opioids?
MR. PENDELL: Objection.
A. I think this partition has been talked -- been asked about previously.
Again, I did not partition on this basis. I don't -- I wouldn't know how to do it. It's not within my expertise. And my assignment was to compute the net economic costs of the total.
Q. Does --
MR. KEYES: Strike that.
Q. Is reduction in pain a benefit of using prescription opioids in accordance with like scientifically acceptable clinical criteria?

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A. Yes, it might be.
Q. Are opioids medically indicated for severe pain associated with trauma?
MR. PENDELL: Objection.
A. This is, of course, outside the expertise of an economist, but I've seen reports that would support that. And I believe some of the medical experts in this case also would agree with that.
Q. Are opioids medically indicated for severe post-surgical pain?
MR. PENDELL: Objection.
A. This is outside the scope of my expertise, but I think that they may be.
Q. Are opioids medically indicated for severe pain associated with cancer end-of-life care?
MR. PENDELL: Objection. Outside the scope.
A. This is outside the scope of my expertise. But they may be.
Q. Could you turn to Paragraph 56 of your report?
MR. PENDELL: Andy, at some point -- you can finish this up. But I want to take a break if we can. We've been going for a while.

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MR. KEYES: Sure. Just give me a few more questions.
MR. PENDELL: No problem. No problem.
Q. Professor, are you at Paragraph 56 of your report?
A. Yes.
Q. Okay.
A. What paragraph -- sorry, wait. I was on page -- hold on.
Q. Yeah, paragraph 56.
MR. PENDELL: Page 32, Professor.
A. Yeah, I'm there.
Q. Okay. Do you see the sentence on the fourth line that says, quote, "Opioids are medically indicated for severe pain associated with trauma, post-surgery and cancer end-of-life care"?
A. Yes, I see that sentence.
Q. And you included that in your report.
A. There it is.
Q. Okay. Do you agree that opioid drugs are more effective than other pain relievers for acute traumatic pain?
MR. PENDELL: Objection.
A. No, that's way outside my area of

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expertise. I'm sorry, I can't give you an opinion about that.
Q. Okay. Do you agree that opioid drugs can be critical for short-term severe pain relief in acute situations?
MR. PENDELL: Objection.
A. Oh, I don't know. They might. It's also outside my area.
Q. Do you agree that in short term acute pain situations such as during surgery or immediately post surgery, prescription opioids can be an important mechanism of pain relief?
MR. PENDELL: Objection.
A. Outside the scope. Maybe.
MR. KEYES: Why don't we take a break.
MR. PENDELL: Thanks.
MR. KEYES: Ten minutes? Go off the record?
MR. PENDELL: Sure.
VIDEO OPERATOR: Going off the record. The time is 10:28 a.m.
(A recess was taken after which the proceedings continued as follows:)
VIDEO OPERATOR: We're back on the

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record. The time is 10:38 a.m. This begins Media Unit 3 in the deposition of Tom McGuire.
BY MR. KEYES:
Q. Professor McGuire, is improvement in function a benefit of using prescription opioids in accordance with scientifically acceptable clinical criteria?
MR. PENDELL: Objection. Outside the scope.
A. That's really outside the scope of my expertise. It may be.
Q. Do opioids help increase the mobility of the patient?
MR. PENDELL: Same objection.
MR. KO: Also object to the form.
A. They -- this is outside my area of expertise. It's kind of a clinical outcome sort of question. I'm not in a position to answer.
Q. Can opioids increase a person's ability to participate in life activities other than working a job?
MR. PENDELL: Objection.
A. This is something else that's outside my expertise. I really wouldn't be in a good position

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to say.
Q. Can opioids be properly used to decrease a patient's anxiety about a surgical procedure?
MR. PENDELL: Objection to form.
A. That's outside my area. I really have no idea.
Q. Can opioids be used to decrease a patient's anxiety about an injury?
MR. PENDELL: Objection.
A. That's outside my area. I have no idea.
Q. Can opioids help allow a patient to have a future perspective that significant pain does not allow?
MR. PENDELL: Objection.
A. Out -- I -- that's not my area. I really -- I have no idea.
Q. Do you agree that the benefits of opioids have been proven useful in palliative care settings?
MR. PENDELL: Objection to form.
A. "Proven" sounds like a statement about randomized controlled trials in these settings, and I -- I'm really not directly familiar with that.
Q. Can prescription opioids be appropriately

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used in the palliative care setting?
MR. PENDELL: Objection. Outside the scope.
A. That's outside my area. I really -- I wouldn't be in a position to say.
Q. Can prescription opioids be appropriately used to address pain experienced by patients with terminal cancer?
MR. PENDELL: Objection to form.
A. Could -- I'm sorry, I wasn't sure I got the wording of that. Would you please provide --
Q. Sure. Sure. Can prescription opioids be appropriately used to address pain experienced by patients with terminal cancer?
MR. PENDELL: Objection.
A. This is outside my area, but they may be.
Q. Can prescription opioids be appropriately used in hospice?
MR. PENDELL: Objection to form.
A. Well, of course, they can -- actually, this is outside my area. I'm just gonna say I really -- I'm not in a position to say.
Q. Did you conduct any research into the benefit of using prescription opioids for hospice

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patients?
A. I would say, no, I did not conduct any such research.
Q. Did you attempt to measure the benefit of using prescription opioids with hospice patients?
A. Well, this is something that I relied on input from clinical experts for. I didn't make an independent determination.
Q. Okay. But did you attempt to measure the benefit of using prescription opioids with hospice patients?
MR. KO: Asked and answered.
A. Well, as I said in the first time this was asked, this was something that I relied on clinical input for, and I didn't make an independent determination.
Q. Did you conduct any research into using prescription opioids to address pain experienced by patients with terminal cancer?
A. I didn't conduct any of my own research on that subject.
Q. Did you attempt to measure the benefit of using prescription opioids to address pain experienced by patients with terminal cancer?

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A. This is -- my answer is similar to the previous set of questions, which is that I relied on clinical input for these matters, and I didn't -- I didn't undertake any independent determination.
Q. Did you attempt to measure the benefit of using opioids in palliative care settings?
A. I also would -- in this context, would have relied on input from clinical experts, and I didn't make any independent determination.
Q. Did you attempt to measure the benefit of using prescription opioids to provide relief from acute pain suffered by mothers who had Caesarean sections?
MR. KO: Object to the form.
A. Could -- would you remind repeating that? I want to make sure I understand the form of what you just asked.
Q. Sure. Did you attempt to measure the benefit from using prescription opioids to provide relief from acute pain being suffered by mothers who had undergone a Caesarean section?
A. This is a clinical area that I relied on inputs from clinicians for my purposes. I didn't

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attempt an independent determination.
Q. Did you attempt to measure the benefit of using prescription opioids to provide relief from acute pain for people who had a root canal?
A. This is the same. Clinical input was what I -- on this subject, is what I took into account. I didn't investigate root canals on my own.
Q. Did you attempt to measure the benefit of using prescription opioids to provide relief from acute pain being suffered by people who had their wisdom teeth extracted?
A. This is, again, an area in which I relied on clinical input. I didn't attempt any independent determination.
Q. Did you attempt to measure the benefit of using prescription opioids to provide relief from acute pain being suffered by people who had orthopedic surgery?
A. This is something I relied on clinical input for. I didn't attempt an independent determination.
Q. Did you attempt to quantify the benefit from using prescription opioids to provide relief from acute pain suffered by patients who had just

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had surgery?
MR. PENDELL: Object to the form.
A. Again, this is a subject I would have relied on clinical input for. I didn't make an independent determination.
Q. Did you attempt to measure the benefit of using prescription opioids to decrease patient anxiety about their injury or a surgical procedure?
MR. PENDELL: Objection to form.
A. This is something I relied on clinical input for. I didn't attempt an independent determination.
Q. Did you attempt to measure the benefit of using prescription opioids to increase a patient's mobility?
A. I relied on clinical input for matters like this. I didn't attempt an independent determination.
Q. Did you attempt to measure the benefit of using prescription opioids to assess a patient's function to improve?
MR. PENDELL: Object to the form.
Asked and answered.
A. You know, I don't -- I'm sorry, I don't

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understand that question.
Q. Yeah, so have you -- did you attempt to measure the benefit of using prescription opioids to help a patient's functional movement improve?
MR. PENDELL: Objection.
A. Sorry. I would have relied on clinical input here. I didn't attempt an independent determination.
Q. And you've said many times now that you would have relied on the judgment of clinical experts. Did I get that right?
MR. PENDELL: Objection.
A. Yeah, with respect to the last series of questions, yes.
Q. Okay. What do you mean you "would have" relied on the judgment of clinical experts?
A. Maybe that conditional "would" could be replaced by "I did rely."
Q. Okay. What do you mean, you did rely on the judgment of the clinical experts?
A. Well, there is a particular section of my report that addresses the issue of net costs of prescription opioids from a clinical point of view, and my understanding is the clinical expert -

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primarily Doctor Lembke - would have considered the questions you asked me.
They would be much better directed to her, and she provided a global answer to the question of whether the net costs -- whether there were net costs in relation to whatever potential benefits there were, and the answer was unequivocal, and the answer was the costs vastly exceeded the benefits.
Q. So you're relying on Doctor Lembke's opinion that the costs vastly outweigh the benefits?
A. I am relying on that opinion, yes.
Q. And does Doctor Lembke offer that opinion on a macro level or on a patient-by-patient level?
MR. PENDELL: To form.
A. Well, the -- you know, the macro is the sum of the patients, so I think she's -- my understanding of what she's done is addressing that for the -- at a macro level, at which is the -- you know, it's the right way in this context to think about the impact of prescription opioids.
Q. Can you point me to where in your report you rely on Doctor Lembke's judgment that the costs

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of prescription opioids vastly outweigh the benefits of prescription opioids?
A. Well, I think beginning on Paragraph 63 of my report, and particularly on Paragraph 64 where it says, "far outweigh the benefits." That's my under -- that's pretty much the same thing.
Q. And -- you just referenced Paragraph 64?
A. Of my report, yes.
Q. Okay. And the excerpt from Doctor Lembke that you're referring to expresses her view "that at a population level, the risks of long-term opioids for chronic pain far outweigh the benefits"?
A. Yes, that's what I'm talking about.
Q. Okay. And here, her view is at a population level, correct?
A. Yes. That's at a population level.
Q. And she's talking about the risks of long-term opioids for chronic pain outweighing the benefits. Correct?
A. That's correct.
Q. Where does Doctor Lembke offer the opinion that the costs of prescription opioids vastly outweigh the benefits of prescription opioids when

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used to treat acute pain rather than chronic pain?
A. Well, I'd have to look back through the quotes here.
Q. Okay. Are you doing that now?
A. I can do that now.
Well, in -- all right. You may not find the word "vastly" in my report, but there's several Lembke statements here that I believe support that, beginning in Paragraph 63.
The Lembke quote, "The best available evidence...found that non-opioid medications" "provide equivalent or greater pain relief, while opioids confer significantly greater risks."
Now, the way I would interpret that statement is that there are less costly ways to get the same benefits, but the cost of risks significantly -- maybe that's not vastly, but significantly exceed the benefits.
And then -- well, I could -- I'm not sure what else you want me to do here, but she goes on to say that in a clinical trial, that there's very little difference between opioids and even a placebo.
Then we talked about Paragraph 64,

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which is that there's -- at the population level, for a very -- at least a very large segment of what's going on here, the risks far outweigh the benefits.
And let me just remind myself what else is going on here with Lembke for one sec.
Okay. I think this paragraph in contrast that I quote in my -- my Paragraph 65 is pretty definitive with respect to the very significant risks associated with prescription opioids in relation to alternatives which are equally effective.
Q. Does Doctor Lembke offer the opinion that opioids are not indicated for acute pain?
A. I -- gosh. Well, I'm -- I'm again looking at this paragraph to refresh myself what I said about Lembke, and there is a sentence in there that said, "Although opioids are indicated for acute pain" -- so she would --
My assumption based on that statement is that she did not say they were not indicated in all circumstances.
Q. Okay. Does -- based on your review and your understanding of what Doctor Lembke has said,

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does Doctor Lembke say that the costs of prescription opioids outweighs the benefits of prescription opioids when prescription opioids are used to treat acute pain?
MR. PENDELL: Objection.
A. Well, I did come to that conclusion from this. Equivalent relief from other less risky alternatives, that would say to me the net benefits are outweighed by the cost.
Q. Are you relying on anything else in these excerpts from Doctor Lembke for your conclusion?
A. I'm relying on Lembke for this. And I also mentioned Waller.
And it's very consistent. You know, there's a -- according to my reading of Waller, there's, you know, a small set of indications, you know, in relation to a very large medical risk.
Q. Are you relying on anyone besides what Doctor Lembke said in her report and what Doctor Waller said in his report?
A. I'm relying on these two clinicians.
Q. Okay. And you are relying on those two clinicians for the proposition that all of the benefits I asked you questions about are outweighed

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by the costs?
MR. PENDELL: Objection.
A. I'm relying on these clinical inputs for the statement that the net costs are positive of prescription opioids.
Q. And did you do any calculation of the benefits of these prescription opioids? Or are you, instead, just relying on what you understand Doctor Lembke and Doctor Waller to have said?
MR. PENDELL: Objection.
A. I'm relying on their opinion that the net -- that the costs outweigh the benefits and that implies to me that the net costs are positive.
Q. And are you relying on anything else besides Doctor Lembke and Doctor Waller for that proposition?
A. No, I'm just relying on -- I'm just relying on those two clinicians.
Q. And therefore having relied on Doctor Lembke and Doctor Waller for that proposition, you did not undertake to try to quantify or measure any of the benefits of using prescription opioids.
MR. PENDELL: Objection, asked and answered.

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MR. KO: Objection.
A. Well, my -- my task here was to estimate the net. And the net is cost minus benefits. So if I know the net -- or I have reliable opinions that the net is on the cost side, then that tells me what I need to know as an economist, and I can then conservatively - as I did in my report - treat that as zero.
Q. Right. So to determine the net cost, you need to determine the costs and the benefits. Correct?
A. Well, that's -- I mean, in a very general way, that would be correct. And there's different realms in which that question is asked here, and one of them is a clinical realm in which I relied on Lembke and Waller.
Q. And on the cost side, you purported to independently measure and quantify those costs.
A. In some case -- well, yes, in much of my report, I did quantify those costs.
Q. And on the benefits side, rather than attempting to measure them, you are relying on Doctors Lembke and Waller for what you understand them to be saying, which is the costs outweigh the

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benefits.
MR. PENDELL: Objection.
A. Well, I'm relying on the clinicians, Lembke and Waller, to consider the clinical benefits and costs of prescription opioids and to come to a determination of - from their perspective - whether the clinical costs outweigh the clinical benefits, and that's how I read their reports.
Q. Turning to the section of your report on mortality, I think starts with Paragraph 38 --
Are you there?
A. Yes.
Q. Okay. And you explain that you rely on Doctor Keyes' estimate of the number of deaths that are due to prescription opioids. Correct?
A. Yes, I see that.
Q. And when you say, "due to prescription opioids," do you mean due to the sale and distribution of prescription opioids, or something else?
A. I mean by the sale and distribution of.
Q. Okay. So you're relying on Doctor Keyes' estimate of the number of deaths that are due to the sale and distribution of prescription opioids?

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A. Yes.
Q. Did you do any independent work yourself to estimate the number of deaths that are due to the sale and distribution of prescription opioids?
A. In this case, I relied on a very good epidemiologist, Professor Keyes, to provide those estimates.
Q. Right. But my question was whether you did any independent work.
A. Oh.
Q. Did you do any independent work yourself to estimate the number of deaths that are due to the sale and distribution of prescription opioids.
MR. PENDELL: Objection to form.
A. Well, the numbers here are ones that Professor Keyes provided. I obviously worked in this area to assess the costs, but the numbers are from Professor Keyes.
Q. Okay. And the numbers that Professor Keyes supplied are -- were originally set out in Table 2 of your report on page 20, correct?
A. That's correct.
Q. Okay. And looking at the numbers in Table 2, when you got these numbers from Professor Keyes,

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did you do anything to see if they seemed reasonable to you?
A. Yes.
Q. What did you do to evaluate whether the numbers that Professor Keyes had supplied seemed reasonable to you?
A. Well, I think I looked at the magnitude overall in terms of what I would have expected for a community of the size of the Cabell community, and then roughly the timing of those.
I'm not surprised that they, you know, peaked in the -- whatever it is, 2017, in accordance with local reports. And I'm also -- I also would have looked at the composition in terms of direct and indirect prescription opioids.
And this also makes sense to me.
Q. So you -- when you got these numbers that are reflected in Table 2 from Professor Keyes, you did look at them, and you did --
A. Yes.
Q. -- some kind of reasonable evaluation yourself?
A. Well, I looked at them and I just, you know, saw -- sort of mentally, you do this -- that

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for which prescription opioids are the proximate cause" "and those for which prescription opioids were the ultimate but not necessarily the proximate cause."

Do you see that?

A. Well, yeah, I was in the wrong paragraph in the appendix. So it will just take me one second, but --

Q. Sure. It's page 17 of your report.

A. Okay, I see that.

Q. Okay. So is it accurate to say that the costs that you've calculated due -- as being due to the sales and distribution of prescription opioids include some costs for which prescription opioids are the proximate cause and some costs for which prescription opioids were not necessarily the proximate cause?

A. I think that's fair to say.

MR. KEYES: I don't have any further questions at this point.

Do any other counsel have questions?

MR. PENDELL: Plaintiffs counsel may. I would like to take a break, but I don't want to interfere with any of the other defendants that may

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have questions.

I mean, Andy, if I knew you were going to be so short, we probably could have skipped lunch. But if I could have five minutes to talk to David for a moment, David Ko, I'd appreciate it.

MR. KEYES: Sure.

MR. KO: And Tom, go ahead and -- if you don't mind, Tom, why don't you just stay on the Zoom. And you don't have to mute if you mind staying for a moment. Okay?

VIDEO OPERATOR: Going off the record, the time is 1:25 p.m.

(A recess was taken after which the proceedings continued as follows:)

VIDEO OPERATOR: This begins Media Unit 5 in the deposition of Tom McGuire. We're back on the record. The time is 1:28 p.m.

EXAMINATION

BY MR. KO:

Q. Hey, Tom --

MR. KO: And just for the record, this is David Ko of Keller Rohrback on behalf of the plaintiffs.

Q. I just have a few follow-up questions

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regarding some of the stuff that Andy Keyes asked you this morning. And I'm going to call him "Andy" just to not confuse him with the expert, the plaintiff's expert, Kathy Keyes. (Zoom audio glitch)

A. Yeah, her beard looks very different than Andy's.

Q. So earlier today and this morning, I think Andy had asked you whether you had measured the benefits of treating patients with prescription opioids. Do you recall that?

A. I do, yes.

Q. And in response to these questions, you generally responded that you were relying on the clinical inputs of other experts, and I believe in particular Doctor Waller and Doctor Lembke. Do you recall that?

A. I do, yes.

Q. And for context - and so the record is clear - the sections of your report that you were discussing these questions that Andy asked was in the Morbidity/OUD or Opioid Use Disorder section of your report, correct?

A. That's correct.

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Q. And just so the record is clear once again, this is Section 3B of your report, I believe, right? And take your time to concretely confirm that.

A. That's correct.

Q. Okay. Now, in that section and with respect to morbidity - and setting aside your reliance on Doctors Lembke and Waller - did you do any other economic analyses to quantify the potential benefit and costs related to prescription opioid use?

A. Yes, I did.

Q. And it appears that you performed an economic analysis of the impact of prescription opioids on workplace productivity; is that correct?

A. That's generally correct, yes.

Q. And can you describe to the Court briefly why you performed this analysis?

A. Well, I was attempting to address the issue of what were the potential economic benefits to prescription opioids, and weigh those against costs in the same domain, the domain here being work force productivity.

And in order to do that, I examined

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 65 / No. 1
March 18, 2016

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Continuing Education Examination available at http://www.cdc.gov/mmwr/cme/conted.html.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CONTENTS

Disclosure of Relationship

The Core Expert Group (CEG) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Pam Archer discloses authorship of the Oklahoma Emergency Department and Urgent Care Clinic Opioid Prescribing Guidelines and the Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office Based Setting; Bonnie Burman discloses authorship of the Ohio Guidelines for Prescribing Opioids for the Treatment of Chronic, Non-Terminal Pain; Jane Ballantyne discloses that she has served as a paid consultant to Cohen Milstein Sellers & Toll, PLLC, and has special advisory committee responsibilities on the Food and Drug Administration (FDA) Risk Evaluation and Mitigation Strategies committee; Phillip Coffin discloses that in 2012 he provided expert testimony to the California State Assembly regarding a bill to expand naloxone access and reports that he is the principal investigator on a research study of methamphetamine dependence that receives donated injectable naltrexone from Alkermes, Inc.; Gary Franklin discloses authorship of the AMDG Interagency Guideline on Prescribing Opioids for Pain; Erin Krebs discloses that she represented the American College of Physicians at a 2014 Food and Drug Administration meeting on Abuse Deterrent Opioid Formulations; Lewis Nelson discloses his ad-hoc membership on the FDA Drug Safety and Risk Management Advisory Committee; Trupti Patel discloses authorship of the Arizona Opioid Prescribing Guidelines; Robert "Chuck" Rich discloses that he was an author of the 2013 American Academy of Family Physicians position paper on opioids and pain management; Joanna Starrels discloses that she received honoraria from the Betty Ford Institute; Thomas Tape discloses that he was an author of the 2013 American College of Physicians policy position paper on prescription drug abuse. CDC provided 100% of the funding for the supplemental evidence review tasks and meeting support. No foundation or industry support was accepted.

The Opioid Guideline Workgroup (OGW) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Anne Burns discloses that she participated in a congressional briefing sponsored by Reps. Carter and DeSaulnier on the pharmacist's role of furnishing Naloxone and that she participates on the National Advisory Board for the Prescription Drug Abuse and Heroin Summit. Chinazo Cunningham discloses that her husband is employed by Quest Diagnostics and Dr. Cunningham was recused from any discussion related to urine drug testing. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Erin Krebs discloses that she served on the CDC Opioid Prescribing Guideline CEG. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG. Greg Terman discloses that he serves as the President of the American Pain Society. Mark Wallace discloses that he served on a Kempharma advisory panel for an abuse-deterrent hydrocodone formulation to treat acute postoperative pain and Dr. Wallace was recused form any discussion related to abuse-deterrent drugs.

The NCIPC Board of Scientific Counselors (BSC) members disclose that they have no financial conflicts of interest. Two BSC members, Traci Green and Christina Porucznik, served on the Opioid Guideline Workgroup. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG.

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Recommendations and Reports

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Prepared by
Deborah Dowell, MD[1]
Tamara M. Haegerich, PhD[1]
Roger Chou, MD[1]
[1]*Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC, Atlanta, Georgia*

Summary

This guideline provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline addresses 1) when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up, and discontinuation; and 3) assessing risk and addressing harms of opioid use. CDC developed the guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework, and recommendations are made on the basis of a systematic review of the scientific evidence while considering benefits and harms, values and preferences, and resource allocation. CDC obtained input from experts, stakeholders, the public, peer reviewers, and a federally chartered advisory committee. It is important that patients receive appropriate pain treatment with careful consideration of the benefits and risks of treatment options. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025) as well as a website (http://www.cdc.gov/drugoverdose/prescribingresources.html) with additional tools to guide clinicians in implementing the recommendations.

Introduction

Background

Opioids are commonly prescribed for pain. An estimated 20% of patients presenting to physician offices with noncancer pain symptoms or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription (*1*). In 2012, health care providers wrote 259 million prescriptions for opioid pain medication, enough for every adult in the United States to have a bottle of pills (*2*). Opioid prescriptions per capita increased 7.3% from 2007 to 2012, with opioid prescribing rates increasing more for family practice, general practice, and internal medicine compared with other specialties (*3*). Rates of opioid prescribing vary greatly across states in ways that cannot be explained by the underlying health status of the population, highlighting the lack of consensus among clinicians on how to use opioid pain medication (*2*).

Prevention, assessment, and treatment of chronic pain are challenges for health providers and systems. Pain might go unrecognized, and patients, particularly members of racial and ethnic minority groups, women, the elderly, persons with cognitive impairment, and those with cancer and at the end of life, can be at risk for inadequate pain treatment (*4*). Patients can experience persistent pain that is not well controlled. There are clinical, psychological, and social consequences associated with chronic pain including limitations in complex activities, lost work productivity, reduced quality of life, and stigma, emphasizing the importance of appropriate and compassionate patient care (*4*). Patients should receive appropriate pain treatment based on a careful consideration of the benefits and risks of treatment options.

Chronic pain has been variably defined but is defined within this guideline as pain that typically lasts >3 months or past the time of normal tissue healing (*5*). Chronic pain can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause (*4*). Estimates of the prevalence of chronic pain vary, but it is clear that the number of persons experiencing chronic pain in the United States is substantial. The 1999–2002 National Health and Nutrition Examination Survey estimated that 14.6% of adults have current widespread or localized pain lasting at least 3 months (*6*). Based on a survey conducted during 2001–2003 (*7*), the overall prevalence of common, predominantly musculoskeletal pain conditions (e.g., arthritis, rheumatism, chronic back or neck problems, and frequent severe headaches) was estimated at 43% among adults in the

Corresponding author: Deborah Dowell, Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC. E-mail: gdo7@cdc.gov.

United States, although minimum duration of symptoms was not specified. Most recently, analysis of data from the 2012 National Health Interview Study showed that 11.2% of adults report having daily pain (*8*). Clinicians should consider the full range of therapeutic options for the treatment of chronic pain. However, it is hard to estimate the number of persons who could potentially benefit from opioid pain medication long term. Evidence supports short-term efficacy of opioids for reducing pain and improving function in noncancer nociceptive and neuropathic pain in randomized clinical trials lasting primarily ≤12 weeks (*9*,*10*), and patients receiving opioid therapy for chronic pain report some pain relief when surveyed (*11*–*13*). However, few studies have been conducted to rigorously assess the long-term benefits of opioids for chronic pain (pain lasting >3 months) with outcomes examined at least 1 year later (*14*). On the basis of data available from health systems, researchers estimate that 9.6–11.5 million adults, or approximately 3%–4% of the adult U.S. population, were prescribed long-term opioid therapy in 2005 (*15*).

Opioid pain medication use presents serious risks, including overdose and opioid use disorder. From 1999 to 2014, more than 165,000 persons died from overdose related to opioid pain medication in the United States (*16*). In the past decade, while the death rates for the top leading causes of death such as heart disease and cancer have decreased substantially, the death rate associated with opioid pain medication has increased markedly (*17*). Sales of opioid pain medication have increased in parallel with opioid-related overdose deaths (*18*). The Drug Abuse Warning Network estimated that >420,000 emergency department visits were related to the misuse or abuse of narcotic pain relievers in 2011, the most recent year for which data are available (*19*). Although clinical criteria have varied over time, opioid use disorder is a problematic pattern of opioid use leading to clinically significant impairment or distress. This disorder is manifested by specific criteria such as unsuccessful efforts to cut down or control use and use resulting in social problems and a failure to fulfill major role obligations at work, school, or home (*20*). This diagnosis has also been referred to as "abuse or dependence" and "addiction" in the literature, and is different from tolerance (diminished response to a drug with repeated use) and physical dependence (adaptation to a drug that produces symptoms of withdrawal when the drug is stopped), both of which can exist without a diagnosed disorder. In 2013, on the basis of DSM-IV diagnosis criteria, an estimated 1.9 million persons abused or were dependent on prescription opioid pain medication (*21*). Having a history of a prescription for an opioid pain medication increases the risk for overdose and opioid use disorder (*22*–*24*), highlighting the value of guidance on safer prescribing practices for clinicians. For example, a recent study of patients aged 15–64 years receiving opioids for chronic noncancer pain and followed for up to 13 years revealed that one in 550 patients died from opioid-related overdose at a median of 2.6 years from their first opioid prescription, and one in 32 patients who escalated to opioid dosages >200 morphine milligram equivalents (MME) died from opioid-related overdose (*25*).

This guideline provides recommendations for the prescribing of opioid pain medication by primary care clinicians for chronic pain (i.e., pain conditions that typically last >3 months or past the time of normal tissue healing) in outpatient settings outside of active cancer treatment, palliative care, and end-of-life care. Although the guideline does not focus broadly on pain management, appropriate use of long-term opioid therapy must be considered within the context of all pain management strategies (including nonopioid pain medications and nonpharmacologic treatments). CDC's recommendations are made on the basis of a systematic review of the best available evidence, along with input from experts, and further review and deliberation by a federally chartered advisory committee. The guideline is intended to ensure that clinicians and patients consider safer and more effective treatment, improve patient outcomes such as reduced pain and improved function, and reduce the number of persons who develop opioid use disorder, overdose, or experience other adverse events related to these drugs. Clinical decision making should be based on a relationship between the clinician and patient, and an understanding of the patient's clinical situation, functioning, and life context. The recommendations in the guideline are voluntary, rather than prescriptive standards. They are based on emerging evidence, including observational studies or randomized clinical trials with notable limitations. Clinicians should consider the circumstances and unique needs of each patient when providing care.

Rationale

Primary care clinicians report having concerns about opioid pain medication misuse, find managing patients with chronic pain stressful, express concern about patient addiction, and report insufficient training in prescribing opioids (*26*). Across specialties, physicians believe that opioid pain medication can be effective in controlling pain, that addiction is a common consequence of prolonged use, and that long-term opioid therapy often is overprescribed for patients with chronic noncancer pain (*27*). These attitudes and beliefs, combined with increasing trends in opioid-related overdose, underscore the need for better clinician guidance on opioid prescribing. Clinical practice guidelines focused on prescribing can improve clinician knowledge, change prescribing practices (*28*), and ultimately benefit patient health.

Professional organizations, states, and federal agencies (e.g., the American Pain Society/American Academy of Pain Medicine, 2009; the Washington Agency Medical Directors Group, 2015; and the U.S. Department of Veterans Affairs/Department of Defense, 2010) have developed guidelines for opioid prescribing (*29–31*). Existing guidelines share some common elements, including dosing thresholds, cautious titration, and risk mitigation strategies such as using risk assessment tools, treatment agreements, and urine drug testing. However, there is considerable variability in the specific recommendations (e.g., range of dosing thresholds of 90 MME/day to 200 MME/day), audience (e.g., primary care clinicians versus specialists), use of evidence (e.g., systematic review, grading of evidence and recommendations, and role of expert opinion), and rigor of methods for addressing conflict of interest (*32*). Most guidelines, especially those that are not based on evidence from scientific studies published in 2010 or later, also do not reflect the most recent scientific evidence about risks related to opioid dosage.

This CDC guideline offers clarity on recommendations based on the most recent scientific evidence, informed by expert opinion and stakeholder and public input. Scientific research has identified high-risk prescribing practices that have contributed to the overdose epidemic (e.g., high-dose prescribing, overlapping opioid and benzodiazepine prescriptions, and extended-release/long-acting [ER/LA] opioids for acute pain) (*24*,*33*,*34*). Using guidelines to address problematic prescribing has the potential to optimize care and improve patient safety based on evidence-based practice (*28*), as well as reverse the cycle of opioid pain medication misuse that contributes to the opioid overdose epidemic.

Scope and Audience

This guideline is intended for primary care clinicians (e.g., family physicians and internists) who are treating patients with chronic pain (i.e., pain lasting >3 months or past the time of normal tissue healing) in outpatient settings. Prescriptions by primary care clinicians account for nearly half of all dispensed opioid prescriptions, and the growth in prescribing rates among these clinicians has been above average (*3*). Primary care clinicians include physicians as well as nurse practitioners and physician assistants. Although the focus is on primary care clinicians, because clinicians work within team-based care, the recommendations refer to and promote integrated pain management and collaborative working relationships with other providers (e.g., behavioral health providers, pharmacists, and pain management specialists). Although the transition from use of opioid therapy for acute pain to use for chronic pain is hard to predict and identify, the guideline is intended to inform clinicians who are considering prescribing opioid pain medication for painful conditions that can or have become chronic.

This guideline is intended to apply to patients aged ≥18 years with chronic pain outside of palliative and end-of-life care. For this guideline, palliative care is defined in a manner consistent with that of the Institute of Medicine as care that provides relief from pain and other symptoms, supports quality of life, and is focused on patients with serious advanced illness. Palliative care can begin early in the course of treatment for any serious illness that requires excellent management of pain or other distressing symptoms (*35*). End-of-life care is defined as care for persons with a terminal illness or at high risk for dying in the near future in hospice care, hospitals, long-term care settings, or at home. Patients within the scope of this guideline include cancer survivors with chronic pain who have completed cancer treatment, are in clinical remission, and are under cancer surveillance only. The guideline is not intended for patients undergoing active cancer treatment, palliative care, or end-of-life care because of the unique therapeutic goals, ethical considerations, opportunities for medical supervision, and balance of risks and benefits with opioid therapy in such care.

The recommendations address the use of opioid pain medication in certain special populations (e.g., older adults and pregnant women) and in populations with conditions posing special risks (e.g., a history of substance use disorder). The recommendations do not address the use of opioid pain medication in children or adolescents aged <18 years. The available evidence concerning the benefits and harms of long-term opioid therapy in children and adolescents is limited, and few opioid medications provide information on the label regarding safety and effectiveness in pediatric patients. However, observational research shows significant increases in opioid prescriptions for pediatric populations from 2001 to 2010 (*36*), and a large proportion of adolescents are commonly prescribed opioid pain medications for conditions such as headache and sports injuries (e.g., in one study, 50% of adolescents presenting with headache received a prescription for an opioid pain medication [*37*,*38*]). Adolescents who misuse opioid pain medication often misuse medications from their own previous prescriptions (*39*), with an estimated 20% of adolescents with currently prescribed opioid medications reporting using them intentionally to get high or increase the effects of alcohol or other drugs (*40*). Use of prescribed opioid pain medication before high school graduation is associated with a 33% increase in the risk of later opioid misuse (*41*). Misuse of opioid pain medications in adolescence strongly predicts later onset of heroin use (*42*). Thus, risk of opioid medication use in pediatric populations is of great concern. Additional clinical trial and observational research is needed,

and encouraged, to inform development of future guidelines for this critical population.

The recommendations are not intended to provide guidance on use of opioids as part of medication-assisted treatment for opioid use disorder. Some of the recommendations might be relevant for acute care settings or other specialists, such as emergency physicians or dentists, but use in these settings or by other specialists is not the focus of this guideline. Readers are referred to other sources for prescribing recommendations within acute care settings and in dental practice, such as the American College of Emergency Physicians' guideline for prescribing of opioids in the emergency department (*43*); the American Society of Anesthesiologists' guideline for acute pain management in the perioperative setting (*44*); the Washington Agency Medical Directors' Group Interagency Guideline on Prescribing Opioids for Pain, Part II: Prescribing Opioids in the Acute and Subacute Phase (*30*); and the Pennsylvania Guidelines on the Use of Opioids in Dental Practice (*45*). In addition, given the challenges of managing the painful complications of sickle cell disease, readers are referred to the NIH National Heart, Lung, and Blood Institute's Evidence Based Management of Sickle Cell Disease Expert Panel Report for management of sickle cell disease (*46*).

Guideline Development Methods

Guideline Development Using the Grading of Recommendations Assessment, Development, and Evaluation Method

CDC developed this guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method (http://www.gradeworkinggroup.org). This method specifies the systematic review of scientific evidence and offers a transparent approach to grading quality of evidence and strength of recommendations. The method has been adapted by the CDC Advisory Committee on Immunization Practices (ACIP) (*47*). CDC has applied the ACIP translation of the GRADE framework in this guideline. Within the ACIP GRADE framework, the body of evidence is categorized in a hierarchy. This hierarchy reflects degree of confidence in the effect of a clinical action on health outcomes. The categories include type 1 evidence (randomized clinical trials or overwhelming evidence from observational studies), type 2 evidence (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 evidence (observational studies or randomized clinical trials with notable limitations), and type 4 evidence (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). Type of evidence is categorized by study design as well as limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and a constellation of plausible biases that could change observations of effects. Type 1 evidence indicates that one can be very confident that the true effect lies close to that of the estimate of the effect; type 2 evidence means that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; type 3 evidence means that confidence in the effect estimate is limited and the true effect might be substantially different from the estimate of the effect; and type 4 evidence indicates that one has very little confidence in the effect estimate, and the true effect is likely to be substantially different from the estimate of the effect (*47*,*48*). When no studies are present, evidence is considered to be insufficient. The ACIP GRADE framework places recommendations in two categories, Category A and Category B. Four major factors determine the category of the recommendation: the quality of evidence, the balance between desirable and undesirable effects, values and preferences, and resource allocation (cost). Category A recommendations apply to all persons in a specified group and indicate that most patients should receive the recommended course of action. Category B recommendations indicate that there should be individual decision making; different choices will be appropriate for different patients, so clinicians must help patients arrive at a decision consistent with patient values and preferences, and specific clinical situations (*47*). According to the GRADE methodology, a particular quality of evidence does not necessarily imply a particular strength of recommendation (*48*–*50*). Category A recommendations can be made based on type 3 or type 4 evidence when the advantages of a clinical action greatly outweigh the disadvantages based on a consideration of benefits and harms, values and preferences, and costs. Category B recommendations are made when the advantages and disadvantages of a clinical action are more balanced. GRADE methodology is discussed extensively elsewhere (*47*,*51*). The U.S. Preventive Services Task Force (USPSTF) follows different methods for developing and categorizing recommendations (http://www.uspreventiveservicestaskforce.org). USPSTF recommendations focus on preventive services and are categorized as A, B, C, D, and I. Under the Affordable Care Act, all "nongrandfathered" health plans (that is, those health plans not in existence prior to March 23, 2010 or those with significant changes to their coverage) and expanded Medicaid plans are required to cover

preventive services recommended by USPSTF with a category A or B rating with no cost sharing. The coverage requirements went into effect September 23, 2010. Similar requirements are in place for vaccinations recommended by ACIP, but do not exist for other recommendations made by CDC, including recommendations within this guideline.

A previously published systematic review sponsored by the Agency for Healthcare Research and Quality (AHRQ) on the effectiveness and risks of long-term opioid treatment of chronic pain (*14*,*52*) initially served to directly inform the recommendation statements. This systematic clinical evidence review addressed the effectiveness of long-term opioid therapy for outcomes related to pain, function, and quality of life; the comparative effectiveness of different methods for initiating and titrating opioids; the harms and adverse events associated with opioids; and the accuracy of risk-prediction instruments and effectiveness of risk mitigation strategies on outcomes related to overdose, addiction, abuse, or misuse. For the current guideline development, CDC conducted additional literature searches to update the evidence review to include more recently available publications and to answer an additional clinical question about the effect of opioid therapy for acute pain on long-term use. More details about the literature search strategies and GRADE methods applied are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026). CDC developed GRADE evidence tables to illustrate the quality of the evidence for each clinical question.

As identified in the AHRQ-sponsored clinical evidence review, the overall evidence base for the effectiveness and risks of long-term opioid therapy is low in quality per the GRADE criteria. Thus, contextual evidence is needed to provide information about the benefits and harms of nonpharmacologic and nonopioid pharmacologic therapy and the epidemiology of opioid pain medication overdose and inform the recommendations. Further, as elucidated by the GRADE Working Group, supplemental information on clinician and patient values and preferences and resource allocation can inform judgments of benefits and harms and be helpful for translating the evidence into recommendations. CDC conducted a contextual evidence review to supplement the clinical evidence review based on systematic searches of the literature. The review focused on the following four areas: effectiveness of nonpharmacologic and nonopioid pharmacologic treatments; benefits and harms related to opioid therapy (including additional studies not included in the clinical evidence review such as studies that evaluated outcomes at any duration or used observational study designs related to specific opioid pain medications, high-dose opioid therapy, co-prescription of opioids with other controlled substances, duration of opioid use, special populations, risk stratification/mitigation approaches, and effectiveness of treatments for addressing potential harms of opioid therapy); clinician and patient values and preferences; and resource allocation. CDC constructed narrative summaries of this contextual evidence and used the information to support the clinical recommendations. More details on methods for the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

On the basis of a review of the clinical and contextual evidence (review methods are described in more detail in subsequent sections of this report), CDC drafted recommendation statements focused on determining when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use. To help assure the draft guideline's integrity and credibility, CDC then began a multistep review process to obtain input from experts, stakeholders, and the public to help refine the recommendations.

Solicitation of Expert Opinion

CDC sought the input of experts to assist in reviewing the evidence and providing perspective on how CDC used the evidence to develop the draft recommendations. These experts, referred to as the "Core Expert Group" (CEG) included subject matter experts, representatives of primary care professional societies and state agencies, and an expert in guideline development methodology.* CDC identified subject matter experts with high scientific standing; appropriate academic and clinical training and relevant clinical experience; and proven scientific excellence in opioid prescribing, substance use disorder treatment, and pain management. CDC identified representatives from leading primary care professional organizations to represent the audience for this guideline. Finally, CDC identified state agency officials and representatives based on their experience with state guidelines for opioid prescribing that were developed with multiple agency stakeholders and informed by scientific literature and existing evidence-based guidelines.

Prior to their participation, CDC asked potential experts to reveal possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Experts could not serve if they had conflicts that might have a direct and predictable effect on the recommendations. CDC excluded experts who had a financial or promotional relationship with a company

* A list of the members appears at the end of this report. The recommendations and all statements included in this guideline are those of CDC and do not necessarily represent the official position of any persons or organizations providing comments on the draft guideline.

that makes a product that might be affected by the guideline. CDC reviewed potential nonfinancial conflicts carefully (e.g., intellectual property, travel, public statements or positions such as congressional testimony) to determine if the activities would have a direct and predictable effect on the recommendations. CDC determined the risk of these types of activities to be minimal for the identified experts. All experts completed a statement certifying that there was no potential or actual conflict of interest. Activities that did not pose a conflict (e.g., participation in Food and Drug Administration [FDA] activities or other guideline efforts) are disclosed.

CDC provided to each expert written summaries of the scientific evidence (both the clinical and contextual evidence reviews conducted for this guideline) and CDC's draft recommendation statements. Experts provided individual ratings for each draft recommendation statement based on the balance of benefits and harms, evidence strength, certainty of values and preferences, cost, recommendation strength, rationale, importance, clarity, and ease of implementation. CDC hosted an in-person meeting of the experts that was held on June 23–24, 2015, in Atlanta, Georgia, to seek their views on the evidence and draft recommendations and to better understand their premeeting ratings. CDC sought the experts' individual opinions at the meeting. Although there was widespread agreement on some of the recommendations, there was disagreement on others. Experts did not vote on the recommendations or seek to come to a consensus. Decisions about recommendations to be included in the guideline, and their rationale, were made by CDC. After revising the guideline, CDC sent written copies of it to each of the experts for review and asked for any additional comments; CDC reviewed these written comments and considered them when making further revisions to the draft guideline. The experts have not reviewed the final version of the guideline.

Federal Partner Engagement

Given the scope of this guideline and the interest of agencies across the federal government in appropriate pain management, opioid prescribing, and related outcomes, CDC invited its National Institute of Occupational Safety and Health and CDC's federal partners to observe the expert meeting, provide written comments on the full draft guideline after the meeting, and review the guideline through an agency clearance process; CDC reviewed comments and incorporated changes. Interagency collaboration will be critical for translating these recommendations into clinical practice. Federal partners included representatives from the Substance Abuse and Mental Health Services Administration, the National Institute on Drug Abuse, FDA, the U.S. Department of Veterans Affairs, the U.S. Department of Defense, the Office of the National Coordinator for Health Information Technology, the Centers for Medicare and Medicaid Services, the Health Resources and Services Administration, AHRQ, and the Office of National Drug Control Policy.

Stakeholder Comment

Given the importance of the guideline for a wide variety of stakeholders, CDC also invited review from a Stakeholder Review Group (SRG) to provide comment so that CDC could consider modifications that would improve the recommendations' specificity, applicability, and ease of implementation. The SRG included representatives from professional organizations that represent specialties that commonly prescribe opioids (e.g., pain medicine, physical medicine and rehabilitation), delivery systems within which opioid prescribing occurs (e.g., hospitals), and representation from community organizations with interests in pain management and opioid prescribing.* Representatives from each of the SRG organizations were provided a copy of the guideline for comment. Each of these representatives provided written comments. Once input was received from the full SRG, CDC reviewed all comments and carefully considered them when revising the draft guideline.

Constituent Engagement

To obtain initial perspectives from constituents on the recommendation statements, including clinicians and prospective patients, CDC convened a constituent engagement webinar and circulated information about the webinar in advance through announcements to partners. CDC hosted the webinar on September 16 and 17, 2015, provided information about the methodology for developing the guideline, and presented the key recommendations. A fact sheet was posted on the CDC Injury Center website (http://www.cdc.gov/injury) summarizing the guideline development process and clinical practice areas addressed in the guideline; instructions were included on how to submit comments via email. CDC received comments during and for 2 days following the first webinar. Over 1,200 constituent comments were received. Comments were reviewed and carefully considered when revising the draft guideline.

Peer Review

Per the final information quality bulletin for peer review (https://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf), peer review requirements applied to this guideline because it provides influential

scientific information that could have a clear and substantial impact on public- and private-sector decisions. Three experts independently reviewed the guideline to determine the reasonableness and strength of recommendations; the clarity with which scientific uncertainties were clearly identified; and the rationale, importance, clarity, and ease of implementation of the recommendations.* CDC selected peer reviewers based on expertise, diversity of scientific viewpoints, and independence from the guideline development process. CDC assessed and managed potential conflicts of interest using a process similar to the one as described for solicitation of expert opinion. No financial interests were identified in the disclosure and review process, and nonfinancial activities were determined to be of minimal risk; thus, no significant conflict of interest concerns were identified. CDC placed the names of peer reviewers on the CDC and the National Center for Injury Prevention and Control Peer Review Agenda websites that are used to provide information about the peer review of influential documents. CDC reviewed peer review comments and revised the draft guideline accordingly.

Public Comment

To obtain comments from the public on the full guideline, CDC published a notice in the *Federal Register* (80 FR 77351) announcing the availability of the guideline and the supporting clinical and contextual evidence reviews for public comment. The comment period closed January 13, 2016. CDC received more than 4,350 comments from the general public, including patients with chronic pain, clinicians, families who have lost loved ones to overdose, medical associations, professional organizations, academic institutions, state and local governments, and industry. CDC reviewed each of the comments and carefully considered them when revising the draft guideline.

Federal Advisory Committee Review and Recommendation

The National Center for Injury Prevention and Control (NCIPC) Board of Scientific Counselors (BSC) is a federal advisory committee that advises and makes recommendations to the Secretary of the Department of Health and Human Services, the Director of CDC, and the Director of NCIPC.* The BSC makes recommendations regarding policies, strategies, objectives, and priorities, and reviews progress toward injury and violence prevention. CDC sought the BSC's advice on the draft guideline. BSC members are special government employees appointed as CDC advisory committee members; as such, all members completed an OGE Form 450 to disclose relevant interests. BSC members also reported on their disclosures during meetings. Disclosures for the BSC are reported in the guideline.

To assist in guideline review, on December 14, 2015, via Federal Register notice, CDC announced the intent to form an Opioid Guideline Workgroup (OGW) to provide observations on the draft guideline to the BSC. CDC provided the BSC with the draft guideline as well as summaries of comments provided to CDC by stakeholders, constituents, and peer reviewers, and edits made to the draft guideline in response. During an open meeting held on January 7, 2016, the BSC recommended the formation of the OGW. The OGW included a balance of perspectives from audiences directly affected by the guideline, audiences that would be directly involved with implementing the recommendations, and audiences qualified to provide representation. The OGW comprised clinicians, subject matter experts, and a patient representative, with the following perspectives represented: primary care, pain medicine, public health, behavioral health, substance abuse treatment, pharmacy, patients, and research.* Additional sought-after attributes were appropriate academic and clinical training and relevant clinical experience; high scientific standing; and knowledge of the patient, clinician, and caregiver perspectives. In accordance with CDC policy, two BSC committee members also served as OGW members, with one serving as the OGW Chair. The professional credentials and interests of OGW members were carefully reviewed to identify possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Only OGW members whose interests were determined to be minimal were selected. When an activity was perceived as having the potential to affect a specific aspect of the recommendations, the activity was disclosed, and the OGW member was recused from discussions related to that specific aspect of the recommendations (e.g., urine drug testing and abuse-deterrent formulations). Disclosures for the OGW are reported. CDC and the OGW identified ad-hoc consultants to supplement the workgroup expertise, when needed, in the areas of pediatrics, occupational medicine, obstetrics and gynecology, medical ethics, addiction psychiatry, physical medicine and rehabilitation, guideline development methodology, and the perspective of a family member who lost a loved one to opioid use disorder or overdose.

The BSC charged the OGW with reviewing the quality of the clinical and contextual evidence reviews and reviewing each of the recommendation statements and accompanying rationales. For each recommendation statement, the OGW considered the quality of the evidence, the balance of benefits and risks, the values and preferences of clinicians and patients, the cost feasibility, and the category designation

of the recommendation (A or B). The OGW also reviewed supplementary documents, including input provided by the CEG, SRG, peer reviewers, and the public. OGW members discussed the guideline accordingly during virtual meetings and drafted a summary report of members' observations, including points of agreement and disagreement, and delivered the report to the BSC.

NCIPC announced an open meeting of the NCIPC BSC in the Federal Register on January 11, 2015. The BSC met on January 28, 2016, to discuss the OGW report and deliberate on the draft guideline itself. Members of the public provided comments at this meeting. After discussing the OGW report, deliberating on specific issues about the draft guideline identified at the meeting, and hearing public comment, the BSC voted unanimously: to support the observations made by the OGW; that CDC adopt the guideline recommendations that, according to the workgroup's report, had unanimous or majority support; and that CDC further consider the guideline recommendations for which the group had mixed opinions. CDC carefully considered the OGW observations, public comments, and BSC recommendations, and revised the guideline in response.

Summary of the Clinical Evidence Review

Primary Clinical Questions

CDC conducted a clinical systematic review of the scientific evidence to identify the effectiveness, benefits, and harms of long-term opioid therapy for chronic pain, consistent with the GRADE approach (*47*,*48*). Long-term opioid therapy is defined as use of opioids on most days for >3 months. A previously published AHRQ-funded systematic review on the effectiveness and risks of long-term opioid therapy for chronic pain comprehensively addressed four clinical questions (*14*,*52*). CDC, with the assistance of a methodology expert, searched the literature to identify newly published studies on these four original questions. Because long-term opioid use might be affected by use of opioids for acute pain, CDC subsequently developed a fifth clinical question (last in the series below), and in collaboration with a methodologist conducted a systematic review of the scientific evidence to address it. In brief, five clinical questions were addressed:

- The effectiveness of long-term opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for long term (≥1 year) outcomes related to pain, function, and quality of life, and how effectiveness varies according to the type/cause of pain, patient demographics, and patient comorbidities (Key Question [KQ] 1).
- The risks of opioids versus placebo or no opioids on abuse, addiction, overdose, and other harms, and how harms vary according to the type/cause of pain, patient demographics, patient comorbidities, and dose (KQ2).
- The comparative effectiveness of opioid dosing strategies (different methods for initiating and titrating opioids; immediate-release versus ER/LA opioids; different ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled, continuous versus as-needed dosing; dose escalation versus dose maintenance; opioid rotation versus maintenance; different strategies for treating acute exacerbations of chronic pain; decreasing opioid doses or tapering off versus continuation; and different tapering protocols and strategies) (KQ3).
- The accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse; the effectiveness of risk mitigation strategies (use of risk prediction instruments); effectiveness of risk mitigation strategies including opioid management plans, patient education, urine drug testing, prescription drug monitoring program (PDMP) data, monitoring instruments, monitoring intervals, pill counts, and abuse-deterrent formulations for reducing risk for opioid overdose, addiction, abuse, or misuse; and the comparative effectiveness of treatment strategies for managing patients with addiction (KQ4).
- The effects of prescribing opioid therapy versus not prescribing opioid therapy for acute pain on long-term use (KQ5).

The review was focused on the effectiveness of long-term opioid therapy on long-term (>1 year) outcomes related to pain, function, and quality of life to ensure that findings are relevant to patients with chronic pain and long-term opioid prescribing. The effectiveness of short-term opioid therapy has already been established (*10*). However, opioids have unique effects such as tolerance and physical dependence that might influence assessments of benefit over time. These effects raise questions about whether findings on short-term effectiveness of opioid therapy can be extrapolated to estimate benefits of long-term therapy for chronic pain. Thus, it is important to consider studies that provide data on long-term benefit. For certain opioid-related harms (overdose, fractures, falls, motor vehicle crashes), observational studies were included with outcomes measured at shorter intervals because such outcomes can occur early during opioid therapy, and such harms are not captured well in short-term clinical trials. A detailed listing of the key questions is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Clinical Evidence Systematic Review Methods

Complete methods and data for the 2014 AHRQ report, upon which this updated systematic review is based, have been published previously (*14*,*52*). Study authors developed the protocol using a standardized process (*53*) with input from experts and the public and registered the protocol in the PROSPERO database (*54*). For the 2014 AHRQ report, a research librarian searched MEDLINE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, PsycINFO, and CINAHL for English-language articles published January 2008 through August 2014, using search terms for opioid therapy, specific opioids, chronic pain, and comparative study designs. Also included were relevant studies from an earlier review (*10*) in which searches were conducted without a date restriction, reference lists were reviewed, and ClinicalTrials.gov was searched. CDC updated the AHRQ literature search using the same search strategies as in the original review including studies published before April, 2015. Seven additional studies met inclusion criteria and were added to the review. CDC used the GRADE approach outlined in the ACIP Handbook for Developing Evidence-Based Recommendations (*47*) to rate the quality of evidence for the full body of evidence (evidence from the 2014 AHRQ review plus the update) for each clinical question. Evidence was categorized into the following types: type 1 (randomized clinical trials or overwhelming evidence from observational studies), type 2 (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 (observational studies, or randomized clinical trials with notable limitations), or type 4 (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). When no studies were present, evidence was considered to be insufficient. Per GRADE methods, type of evidence was categorized by study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects. Results were synthesized qualitatively, highlighting new evidence identified during the update process. Meta-analysis was not attempted due to the small numbers of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of the studies. More detailed information about data sources and searches, study selection, data extraction and quality assessment, data synthesis, and update search yield and new evidence for the current review is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Summary of Findings for Clinical Questions

The main findings of this updated review are consistent with the findings of the 2014 AHRQ report (*14*). In summary, evidence on long-term opioid therapy for chronic pain outside of end-of-life care remains limited, with insufficient evidence to determine long-term benefits versus no opioid therapy, though evidence suggests risk for serious harms that appears to be dose-dependent. These findings supplement findings from a previous review of the effectiveness of opioids for adults with chronic noncancer pain. In this previous review, based on randomized trials predominantly ≤12 weeks in duration, opioids were found to be moderately effective for pain relief, with small benefits for functional outcomes; although estimates vary, based on uncontrolled studies, a high percentage of patients discontinued long-term opioid use because of lack of efficacy and because of adverse events (*10*).

The GRADE evidence summary with type of evidence ratings for the five clinical questions for the current evidence review are outlined (Table 1). This summary is based on studies included in the AHRQ 2014 review (35 studies) plus additional studies identified in the updated search (seven studies). Additional details on findings from the original review are provided in the full 2014 AHRQ report (*14*,*52*). Full details on the clinical evidence review findings supporting this guideline are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Effectiveness

For KQ1, no study of opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for chronic pain evaluated long-term (≥1 year) outcomes related to pain, function, or quality of life. Most placebo-controlled randomized clinical trials were ≤6 weeks in duration. Thus, the body of evidence for KQ1 is rated as insufficient (0 studies contributing) (*14*).

Harms

For KQ2, the body of evidence is rated as type 3 (12 studies contributing; 11 from the original review plus one new study). One fair-quality cohort study found that long-term opioid therapy is associated with increased risk for an opioid abuse or dependence diagnosis (as defined by ICD-9-CM codes) versus no opioid prescription (*22*). Rates of opioid abuse or dependence diagnosis ranged from 0.7% with lower-dose (≤36 MME) chronic therapy to 6.1% with higher-dose (≥120 MME) chronic therapy, versus 0.004% with no opioids prescribed. Ten fair-quality uncontrolled studies reported estimates of opioid abuse, addiction, and related outcomes (*55*–*65*). In primary care settings, prevalence of opioid dependence

(using DSM-IV criteria) ranged from 3% to 26% (*55*,*56*,*59*). In pain clinic settings, prevalence of addiction ranged from 2% to 14% (*57*,*58*,*60*,*61*,*63*–*65*).

Factors associated with increased risk for misuse included history of substance use disorder, younger age, major depression, and use of psychotropic medications (*55*,*62*). Two studies reported on the association between opioid use and risk for overdose (*66*,*67*). One large fair-quality retrospective cohort study found that recent opioid use was associated with increased risk for any overdose events and serious overdose events versus nonuse (*66*). It also found higher doses associated with increased risk. Relative to 1–19 MME/day, the adjusted hazard ratio (HR) for any overdose event (consisting of mostly nonfatal overdose) was 1.44 for 20 to 49 MME/day, 3.73 for 50–99 MME/day, and 8.87 for ≥100 MME/day. A similar pattern was observed for serious overdose. A good-quality population-based, nested case-control study also found a dose-dependent association with risk for overdose death (*67*). Relative to 1–19 MME/day, the adjusted odds ratio (OR) was 1.32 for 20–49 MME/day, 1.92 for 50–99 MME/day, 2.04 for 100–199 MME/day, and 2.88 for ≥200 MME/day.

Findings of increased fracture risk for current opioid use, versus nonuse, were mixed in two studies (*68*,*69*). Two studies found an association between opioid use and increased risk for cardiovascular events (*70*,*71*). Indirect evidence was found for endocrinologic harms (increased use of medications for erectile dysfunction or testosterone from one previously included study; laboratory-defined androgen deficiency from one newly reviewed study) (*72*,*73*). One study found that opioid dosages ≥20 MME/day were associated with increased odds of road trauma among drivers (*74*).

Opioid Dosing Strategies

For KQ3, the body of evidence is rated as type 4 (14 studies contributing; 12 from the original review plus two new studies). For initiation and titration of opioids, the 2014 AHRQ report found insufficient evidence from three fair-quality, open-label trials to determine comparative effectiveness of ER/LA versus immediate-release opioids for titrating patients to stable pain control (*75*,*76*). One new fair-quality cohort study of Veterans Affairs patients found initiation of therapy with an ER/LA opioid associated with greater risk for nonfatal overdose than initiation with an immediate-release opioid, with risk greatest in the first 2 weeks after initiation of treatment (*77*).

For comparative effectiveness and harms of ER/LA opioids, the 2014 AHRQ report included three randomized, head-to-head trials of various ER/LA opioids that found no clear differences in 1-year outcomes related to pain or function (*78*–*80*) but had methodological shortcomings. A fair-quality retrospective cohort study based on national Veterans Health Administration system pharmacy data found that methadone was associated with lower overall risk for all-cause mortality versus morphine (*81*), and a fair-quality retrospective cohort study based on Oregon Medicaid data found no statistically significant differences between methadone and long-acting morphine in risk for death or overdose symptoms (*82*). However, a new observational study (*83*) found methadone associated with increased risk for overdose versus sustained-release morphine among Tennessee Medicaid patients. The observed inconsistency in study findings suggests that risks of methadone might vary in different settings as a function of different monitoring and management protocols, though more research is needed to understand factors associated with safer methadone prescribing.

For dose escalation, the 2014 AHRQ report included one fair-quality randomized trial that found no differences between more liberal dose escalation and maintenance of current doses after 12 months in pain, function, all-cause withdrawals, or withdrawals due to opioid misuse (*84*). However, the difference in opioid dosages prescribed at the end of the trial was relatively small (mean 52 MME/day with more liberal dosing versus 40 MME/day). Evidence on other comparisons related to opioid dosing strategies (ER/LA versus immediate-release opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled continuous dosing versus as-needed dosing; or opioid rotation versus maintenance of current therapy; long-term effects of strategies for treating acute exacerbations of chronic pain) was not available or too limited to determine effects on long-term clinical outcomes. For example, evidence on the comparative effectiveness of opioid tapering or discontinuation versus maintenance, and of different opioid tapering strategies, was limited to small, poor-quality studies (*85*–*87*).

Risk Assessment and Mitigation

For KQ4, the body of evidence is rated as type 3 for the accuracy of risk assessment tools and insufficient for the effectiveness of use of risk assessment tools and mitigation strategies in reducing harms (six studies contributing; four from the original review plus two new studies). The 2014 AHRQ report included four studies (*88*–*91*) on the accuracy of risk assessment instruments, administered prior to opioid therapy initiation, for predicting opioid abuse or misuse. Results for the Opioid Risk Tool (ORT) (*89*–*91*) were extremely inconsistent; evidence for other risk assessment instruments was very sparse, and studies had serious methodological shortcomings. One additional fair-quality (*92*) and one poor-quality (*93*) study identified for this update compared the predictive accuracy of the ORT, the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R), and the Brief Risk Interview.

For the ORT, sensitivity was 0.58 and 0.75 and specificity 0.54 and 0.86; for the SOAPP-R, sensitivity was 0.53 and 0.25 and specificity 0.62 and 0.73; and for the Brief Risk Interview, sensitivity was 0.73 and 0.83 and specificity 0.43 and 0.88. For the ORT, positive likelihood ratios ranged from noninformative (positive likelihood ratio close to 1) to moderately useful (positive likelihood ratio >5). The SOAPP-R was associated with noninformative likelihood ratios (estimates close to 1) in both studies.

No study evaluated the effectiveness of risk mitigation strategies (use of risk assessment instruments, opioid management plans, patient education, urine drug testing, use of PDMP data, use of monitoring instruments, more frequent monitoring intervals, pill counts, or use of abuse-deterrent formulations) for improving outcomes related to overdose, addiction, abuse, or misuse.

Effects of Opioid Therapy for Acute Pain on Long-Term Use

For KQ5, the body of evidence is rated as type 3 (two new studies contributing). Two fair-quality retrospective cohort studies found opioid therapy prescribed for acute pain associated with greater likelihood of long-term use. One study evaluated opioid-naïve patients who had undergone low-risk surgery, such as cataract surgery and varicose vein stripping (*94*). Use of opioids within 7 days of surgery was associated with increased risk for use at 1 year. The other study found that among patients with a workers' compensation claim for acute low back pain, compared to patients who did not receive opioids early after injury (defined as use within 15 days following onset of pain), patients who did receive early opioids had an increased likelihood of receiving five or more opioid prescriptions 30–730 days following onset that increased with greater early exposure. Versus no early opioid use, the adjusted OR was 2.08 (95% CI = 1.55–2.78) for 1–140 MME/day and increased to 6.14 (95% confidence interval [CI] = 4.92–7.66) for ≥450 MME/day (*95*).

Summary of the Contextual Evidence Review

Primary Areas of Focus

Contextual evidence is complementary information that assists in translating the clinical research findings into recommendations. CDC conducted contextual evidence reviews on four topics to supplement the clinical evidence review findings:

- Effectiveness of nonpharmacologic (e.g., cognitive behavioral therapy [CBT], exercise therapy, interventional treatments, and multimodal pain treatment) and nonopioid pharmacologic treatments (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], antidepressants, and anticonvulsants), including studies of any duration.
- Benefits and harms of opioid therapy (including additional studies not included in the clinical evidence review, such as studies that were not restricted to patients with chronic pain, evaluated outcomes at any duration, performed ecological analyses, or used observational study designs other than cohort and case-cohort control studies) related to specific opioids, high-dose therapy, co-prescription with other controlled substances, duration of use, special populations, and potential usefulness of risk stratification/mitigation approaches, in addition to effectiveness of treatments associated with addressing potential harms of opioid therapy (opioid use disorder).
- Clinician and patient values and preferences related to opioids and medication risks, benefits, and use.
- Resource allocation including costs and economic efficiency of opioid therapy and risk mitigation strategies.

CDC also reviewed clinical guidelines that were relevant to opioid prescribing and could inform or complement the CDC recommendations under development (e.g., guidelines on nonpharmacologic and nonopioid pharmacologic treatments and guidelines with recommendations related to specific clinician actions such as urine drug testing or opioid tapering protocols).

Contextual Evidence Review Methods

CDC conducted a contextual evidence review to assist in developing the recommendations by providing an assessment of the balance of benefits and harms, values and preferences, and cost, consistent with the GRADE approach. Given the public health urgency for developing opioid prescribing recommendations, a rapid review was required for the contextual evidence review for the current guideline. Rapid reviews are used when there is a need to streamline the systematic review process to obtain evidence quickly (*96*). Methods used to streamline the process include limiting searches by databases, years, and languages considered, and truncating quality assessment and data abstraction protocols. CDC conducted "rapid reviews" of the contextual evidence on nonpharmacologic and nonopioid pharmacologic treatments, benefits and harms, values and preferences, and resource allocation.

Detailed information about contextual evidence data sources and searches, inclusion criteria, study selection, and

data extraction and synthesis are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). In brief, CDC conducted systematic literature searches to identify original studies, systematic reviews, and clinical guidelines, depending on the topic being searched. CDC also solicited publication referrals from subject matter experts. Given the need for a rapid review process, grey literature (e.g., literature by academia, organizations, or government in the forms of reports, documents, or proceedings not published by commercial publishers) was not systematically searched. Database sources, including MEDLINE, PsycINFO, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews, varied by topic. Multiple reviewers scanned study abstracts identified through the database searches and extracted relevant studies for review. CDC constructed narrative summaries and tables based on relevant articles that met inclusion criteria, which are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

Findings from the contextual reviews provide indirect evidence and should be interpreted accordingly. CDC did not formally rate the quality of evidence for the studies included in the contextual evidence review using the GRADE method. The studies that addressed benefits and harms, values and preferences, and resource allocation most often employed observational methods, used short follow-up periods, and evaluated selected samples. Therefore the strength of the evidence from these contextual review areas was considered to be low, comparable to type 3 or type 4 evidence. The quality of evidence for nonopioid pharmacologic and nonpharmacologic pain treatments was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines (e.g., for treatment of chronic neuropathic pain, low back pain, osteoarthritis, and fibromyalgia). Similarly, the quality of evidence on pharmacologic and psychosocial opioid use disorder treatment was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines.

Summary of Findings for Contextual Areas

Full narrative reviews and tables that summarize key findings from the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

Effectiveness of Nonpharmacologic and Nonopioid Pharmacologic Treatments

Several nonpharmacologic and nonopioid pharmacologic treatments have been shown to be effective in managing chronic pain in studies ranging in duration from 2 weeks to 6 months. For example, CBT that trains patients in behavioral techniques and helps patients modify situational factors and cognitive processes that exacerbate pain has small positive effects on disability and catastrophic thinking (*97*). Exercise therapy can help reduce pain and improve function in chronic low back pain (*98*), improve function and reduce pain in osteoarthritis of the knee (*99*) and hip (*100*), and improve well-being, fibromyalgia symptoms, and physical function in fibromyalgia (*101*). Multimodal and multidisciplinary therapies (e.g., therapies that combine exercise and related therapies with psychologically based approaches) can help reduce pain and improve function more effectively than single modalities (*102*,*103*). Nonopioid pharmacologic approaches used for pain include analgesics such as acetaminophen, NSAIDs, and cyclooxygenase 2 (COX-2) inhibitors; selected anticonvulsants; and selected antidepressants (particularly tricyclics and serotonin and norepinephrine reuptake inhibitors [SNRIs]). Multiple guidelines recommend acetaminophen as first-line pharmacotherapy for osteoarthritis (*104*–*109*) or for low back pain (*110*) but note that it should be avoided in liver failure and that dosage should be reduced in patients with hepatic insufficiency or a history of alcohol abuse (*109*). Although guidelines also recommend NSAIDs as first-line treatment for osteoarthritis or low back pain (*106*,*110*), NSAIDs and COX-2 inhibitors do have risks, including gastrointestinal bleeding or perforation as well as renal and cardiovascular risks (*111*). FDA has recently strengthened existing label warnings that NSAIDs increase risks for heart attack and stroke, including that these risks might increase with longer use or at higher doses (*112*). Several guidelines agree that first- and second-line drugs for neuropathic pain include anticonvulsants (gabapentin or pregabalin), tricyclic antidepressants, and SNRIs (*113*–*116*). Interventional approaches such as epidural injection for certain conditions (e.g., lumbar radiculopathy) can provide short-term improvement in pain (*117*–*119*). Epidural injection has been associated with rare but serious adverse events, including loss of vision, stroke, paralysis, and death (*120*).

Benefits and Harms of Opioid Therapy

Balance between benefits and harms is a critical factor influencing the strength of clinical recommendations. In particular, CDC considered what is known from the epidemiology research about benefits and harms related to specific opioids and formulations, high dose therapy, co-prescription with other controlled substances, duration of use, special populations, and risk stratification and mitigation approaches. Additional information on benefits and harms of long-term opioid therapy from studies meeting rigorous selection criteria is provided in the clinical evidence review (e.g., see KQ2). CDC also considered the number of persons experiencing chronic pain, numbers potentially benefiting

from opioids, and numbers affected by opioid-related harms. A review of these data is presented in the background section of this document, with detailed information provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). Finally, CDC considered the effectiveness of treatments that addressed potential harms of opioid therapy (opioid use disorder).

Regarding specific opioids and formulations, as noted by FDA, there are serious risks of ER/LA opioids, and the indication for this class of medications is for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment in patients for whom other treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain (*121*). Time-scheduled opioid use was associated with substantially higher average daily opioid dosage than as-needed opioid use in one study (*122*). Methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for pain. Methadone has been found to account for as much as a third of opioid-related overdose deaths involving single or multiple drugs in states that participated in the Drug Abuse Warning Network, which was more than any opioid other than oxycodone, despite representing <2% of opioid prescriptions outside of opioid treatment programs in the United States; further, methadone was involved in twice as many single-drug deaths as any other prescription opioid (*123*).

Regarding high-dose therapy, several epidemiologic studies that were excluded from the clinical evidence review because patient samples were not restricted to patients with chronic pain also examined the association between opioid dosage and overdose risk (*23*,*24*,*124*–*126*). Consistent with the clinical evidence review, the contextual review found that opioid-related overdose risk is dose-dependent, with higher opioid dosages associated with increased overdose risk. Two of these studies (*23*,*24*), as well as the two studies in the clinical evidence review (*66*,*67*), evaluated similar MME/day dose ranges for association with overdose risk. In these four studies, compared with opioids prescribed at <20 MME/day, the odds of overdose among patients prescribed opioids for chronic nonmalignant pain were between 1.3 (*67*) and 1.9 (*24*) for dosages of 20 to <50 MME/day, between 1.9 (*67*) and 4.6 (*24*) for dosages of 50 to <100 MME/day, and between 2.0 (*67*) and 8.9 (*66*) for dosages of ≥100 MME/day. Compared with dosages of 1–<20 MME/day, absolute risk difference approximation for 50–<100 MME/day was 0.15% for fatal overdose (*24*) and 1.40% for any overdose (*66*), and for ≥100 MME/day was 0.25% for fatal overdose (*24*) and 4.04% for any overdose (*66*). A recent study of Veterans Health Administration patients with chronic pain found that patients who died of overdoses related to opioids were prescribed higher opioid dosages (mean: 98 MME/day; median: 60 MME/day) than controls (mean: 48 MME/day, median: 25 MME/day) (*127*). Finally, another recent study of overdose deaths among state residents with and without opioid prescriptions revealed that prescription opioid-related overdose mortality rates rose rapidly up to prescribed doses of 200 MME/day, after which the mortality rates continued to increase but grew more gradually (*128*). A listing of common opioid medications and their MME equivalents is provided (Table 2).

Regarding coprescription of opioids with benzodiazepines, epidemiologic studies suggest that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31%–61% of decedents (*67*,*128*,*129*). In one of these studies (*67*), among decedents who received an opioid prescription, those whose deaths were related to opioids were more likely to have obtained opioids from multiple physicians and pharmacies than decedents whose deaths were not related to opioids.

Regarding duration of use, patients can experience tolerance and loss of effectiveness of opioids over time (*130*). Patients who do not experience clinically meaningful pain relief early in treatment (i.e., within 1 month) are unlikely to experience pain relief with longer-term use (*131*).

Regarding populations potentially at greater risk for harm, risk is greater for patients with sleep apnea or other causes of sleep-disordered breathing, patients with renal or hepatic insufficiency, older adults, pregnant women, patients with depression or other mental health conditions, and patients with alcohol or other substance use disorders. Interpretation of clinical data on the effects of opioids on sleep-disordered breathing is difficult because of the types of study designs and methods employed, and there is no clear consensus regarding association with risk for developing obstructive sleep apnea syndrome (*132*). However, opioid therapy can decrease respiratory drive, a high percentage of patients on long-term opioid therapy have been reported to have an abnormal apnea-hypopnea index (*133*), opioid therapy can worsen central sleep apnea in obstructive sleep apnea patients, and it can cause further desaturation in obstructive sleep apnea patients not on continuous positive airway pressure (CPAP) (*31*). Reduced renal or hepatic function can result in greater peak effect and longer duration of action and reduce the dose at which respiratory depression and overdose occurs (*134*). Age-related changes in patients aged ≥65 years, such as reduced renal function and medication clearance, even in the absence of renal disease (*135*), result in a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose. Older adults might also be at increased risk for falls and fractures related to opioids (*136*–*138*). Opioids used

in pregnancy can be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with birth defects, including neural tube defects (*139*,*140*), congenital heart defects (*140*), and gastroschisis (*140*); preterm delivery (*141*), poor fetal growth (*141*), and stillbirth (*141*). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome (*142*). Patients with mental health comorbidities and patients with histories of substance use disorders might be at higher risk than other patients for opioid use disorder (*62*,*143*,*144*). Recent analyses found that depressed patients were at higher risk for drug overdose than patients without depression, particularly at higher opioid dosages, although investigators were unable to distinguish unintentional overdose from suicide attempts (*145*). In case-control and case-cohort studies, substance abuse/dependence was more prevalent among patients experiencing overdose than among patients not experiencing overdose (12% versus 6% [*66*], 40% versus 10% [*24*], and 26% versus 9% [*23*]).

Regarding risk stratification approaches, limited evidence was found regarding benefits and harms. Potential benefits of PDMPs and urine drug testing include the ability to identify patients who might be at higher risk for opioid overdose or opioid use disorder, and help determine which patients will benefit from greater caution and increased monitoring or interventions when risk factors are present. For example, one study found that most fatal overdoses could be identified retrospectively on the basis of two pieces of information, multiple prescribers and high total daily opioid dosage, both important risk factors for overdose (*124*,*146*) that are available to prescribers in the PDMP (*124*). However, limited evaluation of PDMPs at the state level has revealed mixed effects on changes in prescribing and mortality outcomes (*28*). Potential harms of risk stratification include underestimation of risks of opioid therapy when screening tools are not adequately sensitive, as well as potential overestimation of risk, which could lead to inappropriate clinical decisions.

Regarding risk mitigation approaches, limited evidence was found regarding benefits and harms. Although no studies were found to examine prescribing of naloxone with opioid pain medication in primary care settings, naloxone distribution through community-based programs providing prevention services for substance users has been demonstrated to be associated with decreased risk for opioid overdose death at the community level (*147*).

Concerns have been raised that prescribing changes such as dose reduction might be associated with unintended negative consequences, such as patients seeking heroin or other illicitly obtained opioids (*148*) or interference with appropriate pain treatment (*149*). With the exception of a study noting an association between an abuse-deterrent formulation of OxyContin and heroin use, showing that some patients in qualitative interviews reported switching to another opioid, including heroin, for many reasons, including cost and availability as well as ease of use (*150*), CDC did not identify studies evaluating these potential outcomes.

Finally, regarding the effectiveness of opioid use disorder treatments, methadone and buprenorphine for opioid use disorder have been found to increase retention in treatment and to decrease illicit opioid use among patients with opioid use disorder involving heroin (*151*–*153*). Although findings are mixed, some studies suggest that effectiveness is enhanced when psychosocial treatments (e.g., contingency management, community reinforcement, psychotherapeutic counseling, and family therapy) are used in conjunction with medication-assisted therapy; for example, by reducing opioid misuse and increasing retention during maintenance therapy, and improving compliance after detoxification (*154*,*155*).

Clinician and Patient Values and Preferences

Clinician and patient values and preferences can inform how benefits and harms of long-term opioid therapy are weighted and estimate the effort and resources required to effectively provide implementation support. Many physicians lack confidence in their ability to prescribe opioids safely (*156*), to predict (*157*) or detect (*158*) prescription drug abuse, and to discuss abuse with their patients (*158*). Although clinicians have reported favorable beliefs and attitudes about improvements in pain and quality of life attributed to opioids (*159*), most consider prescription drug abuse to be a "moderate" or "big" problem in their community, and large proportions are "very" concerned about opioid addiction (55%) and death (48%) (*160*). Clinicians do not consistently use practices intended to decrease the risk for misuse, such as PDMPs (*161*,*162*), urine drug testing (*163*), and opioid treatment agreements (*164*). This is likely due in part to challenges related to registering for PDMP access and logging into the PDMP (which can interrupt normal clinical workflow if data are not integrated into electronic health record systems) (*165*), competing clinical demands, perceived inadequate time to discuss the rationale for urine drug testing and to order confirmatory testing, and feeling unprepared to interpret and address results (*166*).

Many patients do not have an opinion about "opioids" or know what this term means (*167*). Most are familiar with the term "narcotics." About a third associated "narcotics" with addiction or abuse, and about half feared "addiction" from long-term "narcotic" use (*168*). Most patients taking opioids experience side effects (73% of patients taking hydrocodone for noncancer pain [*11*], 96% of patients taking opioids for chronic pain [*12*]), and side effects, rather than pain relief,

have been found to explain most of the variation in patients' preferences related to taking opioids (*12*). For example, patients taking hydrocodone for noncancer pain commonly reported side effects including dizziness, headache, fatigue, drowsiness, nausea, vomiting, and constipation (*11*). Patients with chronic pain in focus groups emphasized effectiveness of goal setting for increasing motivation and functioning (*168*). Patients taking high dosages report reliance on opioids despite ambivalence about their benefits (*169*) and regardless of pain reduction, reported problems, concerns, side effects, or perceived helpfulness (*13*).

Resource Allocation

Resource allocation (cost) is an important consideration in understanding the feasibility of clinical recommendations. CDC searched for evidence on opioid therapy compared with other treatments; costs of misuse, abuse, and overdose from prescription opioids; and costs of specific risk mitigation strategies (e.g., urine drug testing). Yearly direct and indirect costs related to prescription opioids have been estimated (based on studies published since 2010) to be $53.4 billion for nonmedical use of prescription opioids (*170*); $55.7 billion for abuse, dependence (i.e., opioid use disorder), and misuse of prescription opioids (*171*); and $20.4 billion for direct and indirect costs related to opioid-related overdose alone (*172*). In 2012, total expenses for outpatient prescription opioids were estimated at $9.0 billion, an increase of 120% from 2002 (*173*). Although there are perceptions that opioid therapy for chronic pain is less expensive than more time-intensive nonpharmacologic management approaches, many pain treatments, including acetaminophen, NSAIDs, tricyclic antidepressants, and massage therapy, are associated with lower mean and median annual costs compared with opioid therapy (*174*). COX-2 inhibitors, SNRIs, anticonvulsants, topical analgesics, physical therapy, and CBT are also associated with lower median annual costs compared with opioid therapy (*174*). Limited information was found on costs of strategies to decrease risks associated with opioid therapy; however, urine drug testing, including screening and confirmatory tests, has been estimated to cost $211–$363 per test (*175*).

Recommendations

The recommendations are grouped into three areas for consideration:

- Determining when to initiate or continue opioids for chronic pain.
- Opioid selection, dosage, duration, follow-up, and discontinuation.
- Assessing risk and addressing harms of opioid use.

There are 12 recommendations (Box 1). Each recommendation is followed by a rationale for the recommendation, with considerations for implementation noted. In accordance with the ACIP GRADE process, CDC based the recommendations on consideration of the clinical evidence, contextual evidence (including benefits and harms, values and preferences, resource allocation), and expert opinion. For each recommendation statement, CDC notes the recommendation category (A or B) and the type of the evidence (1, 2, 3, or 4) supporting the statement (Box 2). Expert opinion is reflected within each of the recommendation rationales. While there was not an attempt to reach consensus among experts, experts from the Core Expert Group and from the Opioid Guideline Workgroup ("experts") expressed overall, general support for all recommendations. Where differences in expert opinion emerged for detailed actions within the clinical recommendations or for implementation considerations, CDC notes the differences of opinion in the supporting rationale statements.

Category A recommendations indicate that most patients should receive the recommended course of action; category B recommendations indicate that different choices will be appropriate for different patients, requiring clinicians to help patients arrive at a decision consistent with patient values and preferences and specific clinical situations. Consistent with the ACIP (*47*) and GRADE process (*48*), category A recommendations were made, even with type 3 and 4 evidence, when there was broad agreement that the advantages of a clinical action greatly outweighed the disadvantages based on a consideration of benefits and harms, values and preferences, and resource allocation. Category B recommendations were made when there was broad agreement that the advantages and disadvantages of a clinical action were more balanced, but advantages were significant enough to warrant a recommendation. All recommendations are category A recommendations, with the exception of recommendation 10, which is rated as category B. Recommendations were associated with a range of evidence types, from type 2 to type 4.

In summary, the categorization of recommendations was based on the following assessment:

- No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later (with most placebo-controlled randomized trials ≤6 weeks in duration).
- Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury).
- Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm.

BOX 1. CDC recommendations for prescribing opioids for chronic pain outside of active cancer, palliative, and end-of-life care

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

*All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required); see full guideline for evidence ratings.

BOX 2. Interpretation of recommendation categories and evidence type

Recommendation Categories

Based on evidence type, balance between desirable and undesirable effects, values and preferences, and resource allocation (cost).

Category A recommendation: Applies to all persons; most patients should receive the recommended course of action.

Category B recommendation: Individual decision making needed; different choices will be appropriate for different patients. Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.

Evidence Type

Based on study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects.

Type 1 evidence: Randomized clinical trials or overwhelming evidence from observational studies.

Type 2 evidence: Randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies.

Type 3 evidence: Observational studies or randomized clinical trials with notable limitations.

Type 4 evidence: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

Determining When to Initiate or Continue Opioids for Chronic Pain

1. **Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate (recommendation category: A, evidence type: 3).**

Patients with pain should receive treatment that provides the greatest benefits relative to risks. The contextual evidence review found that many nonpharmacologic therapies, including physical therapy, weight loss for knee osteoarthritis, psychological therapies such as CBT, and certain interventional procedures can ameliorate chronic pain. There is high-quality evidence that exercise therapy (a prominent modality in physical therapy) for hip (*100*) or knee (*99*) osteoarthritis reduces pain and improves function immediately after treatment and that the improvements are sustained for at least 2–6 months. Previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*). Exercise therapy also can help reduce pain and improve function in low back pain and can improve global well-being and physical function in fibromyalgia (*98*,*101*). Multimodal therapies and multidisciplinary biopsychosocial rehabilitation-combining approaches (e.g., psychological therapies with exercise) can reduce long-term pain and disability compared with usual care and compared with physical treatments (e.g., exercise) alone. Multimodal therapies are not always available or reimbursed by insurance and can be time-consuming and costly for patients. Interventional approaches such as arthrocentesis and intraarticular glucocorticoid injection for pain associated with rheumatoid arthritis (*117*) or osteoarthritis (*118*) and subacromial corticosteroid injection for rotator cuff disease (*119*) can provide short-term improvement in pain and function. Evidence is insufficient to determine the extent to which repeated glucocorticoid injection increases potential risks such as articular cartilage changes (in osteoarthritis) and sepsis (*118*). Serious adverse events are rare but have been reported with epidural injection (*120*).

Several nonopioid pharmacologic therapies (including acetaminophen, NSAIDs, and selected antidepressants and anticonvulsants) are effective for chronic pain. In particular, acetaminophen and NSAIDs can be useful for arthritis and low back pain. Selected anticonvulsants such as pregabalin and gabapentin can improve pain in diabetic neuropathy and post-herpetic neuralgia (contextual evidence review). Pregabalin, gabapentin, and carbamazepine are FDA-approved for treatment of certain neuropathic pain conditions, and pregabalin is FDA approved for fibromyalgia management. In patients with or without depression, tricyclic antidepressants and SNRIs provide effective analgesia for neuropathic pain conditions including diabetic neuropathy and post-herpetic neuralgia, often at lower dosages and with a shorter time to onset of effect than for treatment of depression (see contextual evidence review). Tricyclics and SNRIs can also relieve fibromyalgia symptoms. The SNRI duloxetine is FDA-approved for the treatment of diabetic neuropathy and fibromyalgia. Because patients with chronic pain often suffer from concurrent depression (*144*), and depression can exacerbate physical symptoms including pain (*177*), patients with co-occurring pain and depression are especially likely to benefit from antidepressant medication (see Recommendation 8). Nonopioid pharmacologic therapies

are not generally associated with substance use disorder, and the numbers of fatal overdoses associated with nonopioid medications are a fraction of those associated with opioid medications (contextual evidence review). For example, acetaminophen, NSAIDs, and opioid pain medication were involved in 881, 228, and 16,651 pharmaceutical overdose deaths in the United States in 2010 (*178*). However, nonopioid pharmacologic therapies are associated with certain risks, particularly in older patients, pregnant patients, and patients with certain co-morbidities such as cardiovascular, renal, gastrointestinal, and liver disease (see contextual evidence review). For example, acetaminophen can be hepatotoxic at dosages of >3–4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease (*109*). NSAID use has been associated with gastritis, peptic ulcer disease, cardiovascular events (*111*,*112*), and fluid retention, and most NSAIDs (choline magnesium trilisate and selective COX-2 inhibitors are exceptions) interfere with platelet aggregation (*179*). Clinicians should review FDA-approved labeling including boxed warnings before initiating treatment with any pharmacologic therapy.

Although opioids can reduce pain during short-term use, the clinical evidence review found insufficient evidence to determine whether pain relief is sustained and whether function or quality of life improves with long-term opioid therapy (KQ1). While benefits for pain relief, function, and quality of life with long-term opioid use for chronic pain are uncertain, risks associated with long-term opioid use are clearer and significant. Based on the clinical evidence review, long-term opioid use for chronic pain is associated with serious risks including increased risk for opioid use disorder, overdose, myocardial infarction, and motor vehicle injury (KQ2). At a population level, more than 165,000 persons in the United States have died from opioid pain-medication-related overdoses since 1999 (see Contextual Evidence Review).

Integrated pain management requires coordination of medical, psychological, and social aspects of health care and includes primary care, mental health care, and specialist services when needed (*180*). Nonpharmacologic physical and psychological treatments such as exercise and CBT are approaches that encourage active patient participation in the care plan, address the effects of pain in the patient's life, and can result in sustained improvements in pain and function without apparent risks. Despite this, these therapies are not always or fully covered by insurance, and access and cost can be barriers for patients. For many patients, aspects of these approaches can be used even when there is limited access to specialty care. For example, previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*) and maintenance of activity for patients with low back pain (*110*). A randomized trial found no difference in reduced chronic low back pain intensity, frequency or disability between patients assigned to relatively low-cost group aerobics and individual physiotherapy or muscle reconditioning sessions (*181*). Low-cost options to integrate exercise include brisk walking in public spaces or use of public recreation facilities for group exercise. CBT addresses psychosocial contributors to pain and improves function (*97*). Primary care clinicians can integrate elements of a cognitive behavioral approach into their practice by encouraging patients to take an active role in the care plan, by supporting patients in engaging in beneficial but potentially anxiety-provoking activities, such as exercise (*179*), or by providing education in relaxation techniques and coping strategies. In many locations, there are free or low-cost patient support, self-help, and educational community-based programs that can provide stress reduction and other mental health benefits. Patients with more entrenched anxiety or fear related to pain, or other significant psychological distress, can be referred for formal therapy with a mental health specialist (e.g., psychologist, psychiatrist, clinical social worker). Multimodal therapies should be considered for patients not responding to single-modality therapy, and combinations should be tailored depending on patient needs, cost, and convenience.

To guide patient-specific selection of therapy, clinicians should evaluate patients and establish or confirm the diagnosis. Detailed recommendations on diagnosis are provided in other guidelines (*110*,*179*), but evaluation should generally include a focused history, including history and characteristics of pain and potentially contributing factors (e.g., function, psychosocial stressors, sleep) and physical exam, with imaging or other diagnostic testing only if indicated (e.g., if severe or progressive neurologic deficits are present or if serious underlying conditions are suspected) (*110*,*179*). For complex pain syndromes, pain specialty consultation can be considered to assist with diagnosis as well as management. Diagnosis can help identify disease-specific interventions to reverse or ameliorate pain; for example, improving glucose control to prevent progression of diabetic neuropathy; immune-modulating agents for rheumatoid arthritis; physical or occupational therapy to address posture, muscle weakness, or repetitive occupational motions that contribute to musculoskeletal pain; or surgical intervention to relieve mechanical/compressive pain (*179*). The underlying mechanism for most pain syndromes can be categorized as neuropathic (e.g., diabetic neuropathy, postherpetic neuralgia, fibromyalgia), or nociceptive (e.g., osteoarthritis, muscular back pain). The diagnosis and pathophysiologic mechanism of pain have implications for symptomatic pain treatment with medication. For example, evidence is limited or insufficient

for improved pain or function with long-term use of opioids for several chronic pain conditions for which opioids are commonly prescribed, such as low back pain (*182*), headache (*183*), and fibromyalgia (*184*). Although NSAIDs can be used for exacerbations of nociceptive pain, other medications (e.g., tricyclics, selected anticonvulsants, or transdermal lidocaine) generally are recommended for neuropathic pain. In addition, improvement of neuropathic pain can begin weeks or longer after symptomatic treatment is initiated (*179*). Medications should be used only after assessment and determination that expected benefits outweigh risks given patient-specific factors. For example, clinicians should consider falls risk when selecting and dosing potentially sedating medications such as tricyclics, anticonvulsants, or opioids, and should weigh risks and benefits of use, dose, and duration of NSAIDs when treating older adults as well as patients with hypertension, renal insufficiency, or heart failure, or those with risk for peptic ulcer disease or cardiovascular disease. Some guidelines recommend topical NSAIDs for localized osteoarthritis (e.g., knee osteoarthritis) over oral NSAIDs in patients aged ≥75 years to minimize systemic effects (*176*).

Experts agreed that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue >3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care, given small to moderate short-term benefits, uncertain long-term benefits, and potential for serious harms; although evidence on long-term benefits of nonopioid therapies is also limited, these therapies are also associated with short-term benefits, and risks are much lower. This does not mean that patients should be required to sequentially "fail" nonpharmacologic and nonopioid pharmacologic therapy before proceeding to opioid therapy. Rather, expected benefits specific to the clinical context should be weighed against risks before initiating therapy. In some clinical contexts (e.g., headache or fibromyalgia), expected benefits of initiating opioids are unlikely to outweigh risks regardless of previous nonpharmacologic and nonopioid pharmacologic therapies used. In other situations (e.g., serious illness in a patient with poor prognosis for return to previous level of function, contraindications to other therapies, and clinician and patient agreement that the overriding goal is patient comfort), opioids might be appropriate regardless of previous therapies used. In addition, when opioid pain medication is used, it is more likely to be effective if integrated with nonpharmacologic therapy. Nonpharmacologic approaches such as exercise and CBT should be used to reduce pain and improve function in patients with chronic pain. Nonopioid pharmacologic therapy should be used when benefits outweigh risks and should be combined with nonpharmacologic therapy to reduce pain and improve function. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate, to provide greater benefits to patients in improving pain and function.

2. **Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine long-term benefits of opioid therapy for chronic pain and found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent. In addition, studies on currently available risk assessment instruments were sparse and showed inconsistent results (KQ4). The clinical evidence review for the current guideline considered studies with outcomes examined at ≥1 year that compared opioid use versus nonuse or placebo. Studies of opioid therapy for chronic pain that did not have a nonopioid control group have found that although many patients discontinue opioid therapy for chronic noncancer pain due to adverse effects or insufficient pain relief, there is weak evidence that patients who are able to continue opioid therapy for at least 6 months can experience clinically significant pain relief and insufficient evidence that function or quality of life improves (*185*). These findings suggest that it is very difficult for clinicians to predict whether benefits of opioids for chronic pain will outweigh risks of ongoing treatment for individual patients. Opioid therapy should not be initiated without consideration of an "exit strategy" to be used if the therapy is unsuccessful.

Experts agreed that before opioid therapy is initiated for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should determine how effectiveness will be evaluated and should establish treatment goals with patients. Because the line between acute pain and initial chronic pain is not always clear, it might be difficult for clinicians to determine when they are initiating opioids for chronic pain rather than treating acute pain. Pain lasting longer than 3 months or past the time of normal tissue healing (which could be substantially shorter than 3 months, depending on the condition) is generally no longer considered acute. However, establishing treatment goals with a patient who has already received opioid therapy for 3 months would defer this discussion well past the point of

initiation of opioid therapy for chronic pain. Clinicians often write prescriptions for long-term use in 30-day increments, and opioid prescriptions written for ≥30 days are likely to represent initiation or continuation of long-term opioid therapy. Before writing an opioid prescription for ≥30 days, clinicians should establish treatment goals with patients. Clinicians seeing new patients already receiving opioids should establish treatment goals for continued opioid therapy. Although the clinical evidence review did not find studies evaluating the effectiveness of written agreements or treatment plans (KQ4), clinicians and patients who set a plan in advance will clarify expectations regarding how opioids will be prescribed and monitored, as well as situations in which opioids will be discontinued or doses tapered (e.g., if treatment goals are not met, opioids are no longer needed, or adverse events put the patient at risk) to improve patient safety.

Experts thought that goals should include improvement in both pain relief and function (and therefore in quality of life). However, there are some clinical circumstances under which reductions in pain without improvement in physical function might be a more realistic goal (e.g., diseases typically associated with progressive functional impairment or catastrophic injuries such as spinal cord trauma). Experts noted that function can include emotional and social as well as physical dimensions. In addition, experts emphasized that mood has important interactions with pain and function. Experts agreed that clinicians may use validated instruments such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) to track patient outcomes. Clinically meaningful improvement has been defined as a 30% improvement in scores for both pain and function (*187*). Monitoring progress toward patient-centered functional goals (e.g., walking the dog or walking around the block, returning to part-time work, attending family sports or recreational activities) can also contribute to the assessment of functional improvement. Clinicians should use these goals in assessing benefits of opioid therapy for individual patients and in weighing benefits against risks of continued opioid therapy (see Recommendation 7, including recommended intervals for follow-up). Because depression, anxiety, and other psychological co-morbidities often coexist with and can interfere with resolution of pain, clinicians should use validated instruments to assess for these conditions (see Recommendation 8) and ensure that treatment for these conditions is optimized. If patients receiving opioid therapy for chronic pain do not experience meaningful improvements in both pain and function compared with prior to initiation of opioid therapy, clinicians should consider working with patients to taper and discontinue opioids (see Recommendation 7) and should use nonpharmacologic and nonopioid pharmacologic approaches to pain management (see Recommendation 1).

3. **Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy (recommendation category: A, evidence type: 3).**

The clinical evidence review did not find studies evaluating effectiveness of patient education or opioid treatment plans as risk-mitigation strategies (KQ4). However, the contextual evidence review found that many patients lack information about opioids and identified concerns that some clinicians miss opportunities to effectively communicate about safety. Given the substantial evidence gaps on opioids, uncertain benefits of long-term use, and potential for serious harms, patient education and discussion before starting opioid therapy are critical so that patient preferences and values can be understood and used to inform clinical decisions. Experts agreed that essential elements to communicate to patients before starting and periodically during opioid therapy include realistic expected benefits, common and serious harms, and expectations for clinician and patient responsibilities to mitigate risks of opioid therapy.

Clinicians should involve patients in decisions about whether to start or continue opioid therapy. Given potentially serious risks of long-term opioid therapy, clinicians should ensure that patients are aware of potential benefits of, harms of, and alternatives to opioids before starting or continuing opioid therapy. Clinicians are encouraged to have open and honest discussions with patients to inform mutual decisions about whether to start or continue opioid therapy. Important considerations include the following:

- Be explicit and realistic about expected benefits of opioids, explaining that while opioids can reduce pain during short-term use, there is no good evidence that opioids improve pain or function with long-term use, and that complete relief of pain is unlikely (clinical evidence review, KQ1).
- Emphasize improvement in function as a primary goal and that function can improve even when pain is still present.
- Advise patients about serious adverse effects of opioids, including potentially fatal respiratory depression and development of a potentially serious lifelong opioid use disorder that can cause distress and inability to fulfill major role obligations.
- Advise patients about common effects of opioids, such as constipation, dry mouth, nausea, vomiting, drowsiness, confusion, tolerance, physical dependence, and withdrawal symptoms when stopping opioids. To prevent constipation associated with opioid use, advise patients to increase

hydration and fiber intake and to maintain or increase physical activity. Stool softeners or laxatives might be needed.
- Discuss effects that opioids might have on ability to safely operate a vehicle, particularly when opioids are initiated, when dosages are increased, or when other central nervous system depressants, such as benzodiazepines or alcohol, are used concurrently.
- Discuss increased risks for opioid use disorder, respiratory depression, and death at higher dosages, along with the importance of taking only the amount of opioids prescribed, i.e., not taking more opioids or taking them more often.
- Review increased risks for respiratory depression when opioids are taken with benzodiazepines, other sedatives, alcohol, illicit drugs such as heroin, or other opioids.
- Discuss risks to household members and other individuals if opioids are intentionally or unintentionally shared with others for whom they are not prescribed, including the possibility that others might experience overdose at the same or at lower dosage than prescribed for the patient, and that young children are susceptible to unintentional ingestion. Discuss storage of opioids in a secure, preferably locked location and options for safe disposal of unused opioids (*188*).
- Discuss the importance of periodic reassessment to ensure that opioids are helping to meet patient goals and to allow opportunities for opioid discontinuation and consideration of additional nonpharmacologic or nonopioid pharmacologic treatment options if opioids are not effective or are harmful.
- Discuss planned use of precautions to reduce risks, including use of prescription drug monitoring program information (see Recommendation 9) and urine drug testing (see Recommendation 10). Consider including discussion of naloxone use for overdose reversal (see Recommendation 8).
- Consider whether cognitive limitations might interfere with management of opioid therapy (for older adults in particular) and, if so, determine whether a caregiver can responsibly co-manage medication therapy. Discuss the importance of reassessing safer medication use with both the patient and caregiver.

Given the possibility that benefits of opioid therapy might diminish or that risks might become more prominent over time, it is important that clinicians review expected benefits and risks of continued opioid therapy with patients periodically, at least every 3 months (see Recommendation 7).

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids (recommendation category: A, evidence type: 4).

ER/LA opioids include methadone, transdermal fentanyl, and extended-release versions of opioids such as oxycodone, oxymorphone, hydrocodone, and morphine. The clinical evidence review found a fair-quality study showing a higher risk for overdose among patients initiating treatment with ER/LA opioids than among those initiating treatment with immediate-release opioids (*77*). The clinical evidence review did not find evidence that continuous, time-scheduled use of ER/LA opioids is more effective or safer than intermittent use of immediate-release opioids or that time-scheduled use of ER/LA opioids reduces risks for opioid misuse or addiction (KQ3).

In 2014, the FDA modified the labeling for ER/LA opioid pain medications, noting serious risks and recommending that ER/LA opioids be reserved for "management of pain severe enough to require daily, around-the-clock, long-term opioid treatment" when "alternative treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain" and not used as "as needed" pain relievers (*121*). FDA has also noted that some ER/LA opioids are only appropriate for opioid-tolerant patients, defined as patients who have received certain dosages of opioids (e.g., 60 mg daily of oral morphine, 30 mg daily of oral oxycodone, or equianalgesic dosages of other opioids) for at least 1 week (*189*). Time-scheduled opioid use can be associated with greater total average daily opioid dosage compared with intermittent, as-needed opioid use (contextual evidence review). In addition, experts indicated that there was not enough evidence to determine the safety of using immediate-release opioids for breakthrough pain when ER/LA opioids are used for chronic pain outside of active cancer pain, palliative care, or end-of-life care, and that this practice might be associated with dose escalation.

Abuse-deterrent technologies have been employed to prevent manipulation intended to defeat extended-release properties of ER/LA opioids and to prevent opioid use by unintended routes of administration, such as injection of oral opioids. As indicated in FDA guidance for industry on evaluation and labeling of abuse-deterrent opioids (*190*), although abuse-deterrent technologies are expected to make manipulation of opioids more difficult or less rewarding, they do not prevent

opioid abuse through oral intake, the most common route of opioid abuse, and can still be abused by nonoral routes. The "abuse-deterrent" label does not indicate that there is no risk for abuse. No studies were found in the clinical evidence review assessing the effectiveness of abuse-deterrent technologies as a risk mitigation strategy for deterring or preventing abuse. In addition, abuse-deterrent technologies do not prevent unintentional overdose through oral intake. Experts agreed that recommendations could not be offered at this time related to use of abuse-deterrent formulations.

In comparing different ER/LA formulations, the clinical evidence review found inconsistent results for overdose risk with methadone versus other ER/LA opioids used for chronic pain (KQ3). The contextual evidence review found that methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for chronic pain. In addition, methadone is associated with cardiac arrhythmias along with QT prolongation on the electrocardiogram, and it has complicated pharmacokinetics and pharmacodynamics, including a long and variable half-life and peak respiratory depressant effect occurring later and lasting longer than peak analgesic effect. Experts noted that the pharmacodynamics of methadone are subject to more inter-individual variability than other opioids. In regard to other ER/LA opioid formulations, experts noted that the absorption and pharmacodynamics of transdermal fentanyl are complex, with gradually increasing serum concentration during the first part of the 72-hour dosing interval, as well as variable absorption based on factors such as external heat. In addition, the dosing of transdermal fentanyl in mcg/hour, which is not typical for a drug used by outpatients, can be confusing. Experts thought that these complexities might increase the risk for fatal overdose when methadone or transdermal fentanyl is prescribed to a patient who has not used it previously or by clinicians who are not familiar with its effects.

Experts agreed that for patients not already receiving opioids, clinicians should not initiate opioid treatment with ER/LA opioids and should not prescribe ER/LA opioids for intermittent use. ER/LA opioids should be reserved for severe, continuous pain and should be considered only for patients who have received immediate-release opioids daily for at least 1 week. When changing to an ER/LA opioid for a patient previously receiving a different immediate-release opioid, clinicians should consult product labeling and reduce total daily dosage to account for incomplete opioid cross-tolerance. Clinicians should use additional caution with ER/LA opioids and consider a longer dosing interval when prescribing to patients with renal or hepatic dysfunction because decreased clearance of drugs among these patients can lead to accumulation of drugs to toxic levels and persistence in the body for longer durations. Although there might be situations in which clinicians need to prescribe immediate-release and ER/LA opioids together (e.g., transitioning patients from ER/LA opioids to immediate-release opioids by temporarily using lower dosages of both), in general, avoiding the use of immediate-release opioids in combination with ER/LA opioids is preferable, given potentially increased risk and diminishing returns of such an approach for chronic pain.

When an ER/LA opioid is prescribed, using one with predictable pharmacokinetics and pharmacodynamics is preferred to minimize unintentional overdose risk. In particular, unusual characteristics of methadone and of transdermal fentanyl make safe prescribing of these medications for pain especially challenging.

- Methadone should not be the first choice for an ER/LA opioid. Only clinicians who are familiar with methadone's unique risk profile and who are prepared to educate and closely monitor their patients, including risk assessment for QT prolongation and consideration of electrocardiographic monitoring, should consider prescribing methadone for pain. A clinical practice guideline that contains further guidance regarding methadone prescribing for pain has been published previously (*191*).
- Because dosing effects of transdermal fentanyl are often misunderstood by both clinicians and patients, only clinicians who are familiar with the dosing and absorption properties of transdermal fentanyl and are prepared to educate their patients about its use should consider prescribing it.

5. **When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day (recommendation category: A, evidence type: 3).**

Benefits of high-dose opioids for chronic pain are not established. The clinical evidence review found only one study (*84*) addressing effectiveness of dose titration for outcomes related to pain control, function, and quality of life (KQ3). This randomized trial found no difference in pain or function between a more liberal opioid dose escalation strategy and maintenance of current dosage. (These groups were prescribed average dosages of 52 and 40 MME/day, respectively, at the end of the trial.) At the same time, risks for serious harms

related to opioid therapy increase at higher opioid dosage. The clinical evidence review found that higher opioid dosages are associated with increased risks for motor vehicle injury, opioid use disorder, and overdose (KQ2). The clinical and contextual evidence reviews found that opioid overdose risk increases in a dose-response manner, that dosages of 50–<100 MME/day have been found to increase risks for opioid overdose by factors of 1.9 to 4.6 compared with dosages of 1–<20 MME/day, and that dosages ≥100 MME/day are associated with increased risks of overdose 2.0–8.9 times the risk at 1–<20 MME/day. In a national sample of Veterans Health Administration patients with chronic pain who were prescribed opioids, mean prescribed opioid dosage among patients who died from opioid overdose was 98 MME (median 60 MME) compared with mean prescribed opioid dosage of 48 MME (median 25 MME) among patients not experiencing fatal overdose (*127*).

The contextual evidence review found that although there is not a single dosage threshold below which overdose risk is eliminated, holding dosages <50 MME/day would likely reduce risk among a large proportion of patients who would experience fatal overdose at higher prescribed dosages. Experts agreed that lower dosages of opioids reduce the risk for overdose, but that a single dosage threshold for safe opioid use could not be identified. Experts noted that daily opioid dosages close to or greater than 100 MME/day are associated with significant risks, that dosages <50 MME/day are safer than dosages of 50–100 MME/day, and that dosages <20 MME/day are safer than dosages of 20–50 MME/day. One expert thought that a specific dosage at which the benefit/risk ratio of opioid therapy decreases could not be identified. Most experts agreed that, in general, increasing dosages to 50 or more MME/day increases overdose risk without necessarily adding benefits for pain control or function and that clinicians should carefully reassess evidence of individual benefits and risks when considering increasing opioid dosages to ≥50 MME/day. Most experts also agreed that opioid dosages should not be increased to ≥90 MME/day without careful justification based on diagnosis and on individualized assessment of benefits and risks.

When opioids are used for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should start opioids at the lowest possible effective dosage (the lowest starting dosage on product labeling for patients not already taking opioids and according to product labeling guidance regarding tolerance for patients already taking opioids). Clinicians should use additional caution when initiating opioids for patients aged ≥65 years and for patients with renal or hepatic insufficiency because decreased clearance of drugs in these patients can result in accumulation of drugs to toxic levels. Clinicians should use caution when increasing opioid dosages and increase dosage by the smallest practical amount because overdose risk increases with increases in opioid dosage. Although there is limited evidence to recommend specific intervals for dosage titration, a previous guideline recommended waiting at least five half-lives before increasing dosage and waiting at least a week before increasing dosage of methadone to make sure that full effects of the previous dosage are evident (*31*). Clinicians should re-evaluate patients after increasing dosage for changes in pain, function, and risk for harm (see Recommendation 7). Before increasing total opioid dosage to ≥50 MME/day, clinicians should reassess whether opioid treatment is meeting the patient's treatment goals (see Recommendation 2). If a patient's opioid dosage for all sources of opioids combined reaches or exceeds 50 MME/day, clinicians should implement additional precautions, including increased frequency of follow-up (see Recommendation 7) and considering offering naloxone and overdose prevention education to both patients and the patients' household members (see Recommendation 8). Clinicians should avoid increasing opioid dosages to ≥90 MME/day or should carefully justify a decision to increase dosage to ≥90 MME/day based on individualized assessment of benefits and risks and weighing factors such as diagnosis, incremental benefits for pain and function relative to harms as dosages approach 90 MME/day, other treatments and effectiveness, and recommendations based on consultation with pain specialists. If patients do not experience improvement in pain and function at ≥90 MME/day, or if there are escalating dosage requirements, clinicians should discuss other approaches to pain management with the patient, consider working with patients to taper opioids to a lower dosage or to taper and discontinue opioids (see Recommendation 7), and consider consulting a pain specialist. Some states require clinicians to implement clinical protocols at specific dosage levels. For example, before increasing long-term opioid therapy dosage to >120 MME/day, clinicians in Washington state must obtain consultation from a pain specialist who agrees that this is indicated and appropriate (*30*). Clinicians should be aware of rules related to MME thresholds and associated clinical protocols established by their states.

Established patients already taking high dosages of opioids, as well as patients transferring from other clinicians, might consider the possibility of opioid dosage reduction to be anxiety-provoking, and tapering opioids can be especially challenging after years on high dosages because of physical and psychological dependence. However, these patients should be offered the opportunity to re-evaluate their continued use of opioids at high dosages in light of recent evidence regarding the association of opioid dosage and overdose risk. Clinicians should explain in a nonjudgmental manner to patients already taking high opioid dosages (≥90 MME/day) that there is

now an established body of scientific evidence showing that overdose risk is increased at higher opioid dosages. Clinicians should empathically review benefits and risks of continued high-dosage opioid therapy and should offer to work with the patient to taper opioids to safer dosages. For patients who agree to taper opioids to lower dosages, clinicians should collaborate with the patient on a tapering plan (see Recommendation 7). Experts noted that patients tapering opioids after taking them for years might require very slow opioid tapers as well as pauses in the taper to allow gradual accommodation to lower opioid dosages. Clinicians should remain alert to signs of anxiety, depression, and opioid use disorder (see Recommendations 8 and 12) that might be unmasked by an opioid taper and arrange for management of these co-morbidities. For patients agreeing to taper to lower opioid dosages as well as for those remaining on high opioid dosages, clinicians should establish goals with the patient for continued opioid therapy (see Recommendation 2), maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1), and consider consulting a pain specialist as needed to assist with pain management.

6. **Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed (recommendation category: A, evidence type: 4).**

The clinical evidence review found that opioid use for acute pain (i.e., pain with abrupt onset and caused by an injury or other process that is not ongoing) is associated with long-term opioid use, and that a greater amount of early opioid exposure is associated with greater risk for long-term use (KQ5). Several guidelines on opioid prescribing for acute pain from emergency departments (*192*–*194*) and other settings (*195*,*196*) have recommended prescribing ≤3 days of opioids in most cases, whereas others have recommended ≤7 days (*197*) or <14 days (*30*). Because physical dependence on opioids is an expected physiologic response in patients exposed to opioids for more than a few days (contextual evidence review), limiting days of opioids prescribed also should minimize the need to taper opioids to prevent distressing or unpleasant withdrawal symptoms. Experts noted that more than a few days of exposure to opioids significantly increases hazards, that each day of unnecessary opioid use increases likelihood of physical dependence without adding benefit, and that prescriptions with fewer days' supply will minimize the number of pills available for unintentional or intentional diversion.

Experts agreed that when opioids are needed for acute pain, clinicians should prescribe opioids at the lowest effective dose and for no longer than the expected duration of pain severe enough to require opioids to minimize unintentional initiation of long-term opioid use. The lowest effective dose can be determined using product labeling as a starting point with calibration as needed based on the severity of pain and on other clinical factors such as renal or hepatic insufficiency (see Recommendation 8). Experts thought, based on clinical experience regarding anticipated duration of pain severe enough to require an opioid, that in most cases of acute pain not related to surgery or trauma, a ≤3 days' supply of opioids will be sufficient. For example, in one study of the course of acute low back pain (not associated with malignancies, infections, spondylarthropathies, fractures, or neurological signs) in a primary care setting, there was a large decrease in pain until the fourth day after treatment with paracetamol, with smaller decreases thereafter (*198*). Some experts thought that because some types of acute pain might require more than 3 days of opioid treatment, it would be appropriate to recommend a range of ≤3–5 days or ≤3–7 days when opioids are needed. Some experts thought that a range including 7 days was too long given the expected course of severe acute pain for most acute pain syndromes seen in primary care.

Acute pain can often be managed without opioids. It is important to evaluate the patient for reversible causes of pain, for underlying etiologies with potentially serious sequelae, and to determine appropriate treatment. When the diagnosis and severity of nontraumatic, nonsurgical acute pain are reasonably assumed to warrant the use of opioids, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids, often 3 days or less, unless circumstances clearly warrant additional opioid therapy. More than 7 days will rarely be needed. Opioid treatment for post-surgical pain is outside the scope of this guideline but has been addressed elsewhere (*30*). Clinicians should not prescribe additional opioids to patients "just in case" pain continues longer than expected. Clinicians should re-evaluate the subset of patients who experience severe acute pain that continues longer than the expected duration to confirm or revise the initial diagnosis and to adjust management accordingly. Given longer half-lives and longer duration of effects (e.g., respiratory depression) with ER/LA opioids such as methadone, fentanyl patches, or extended release versions of opioids such as oxycodone, oxymorphone, or morphine, clinicians should not prescribe ER/LA opioids for the treatment of acute pain.

7. **Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids (recommendation category: A, evidence type: 4).**

Although the clinical evidence review did not find studies evaluating the effectiveness of more frequent monitoring intervals (KQ4), it did find that continuing opioid therapy for 3 months substantially increases risk for opioid use disorder (KQ2); therefore, follow-up earlier than 3 months might be necessary to provide the greatest opportunity to prevent the development of opioid use disorder. In addition, risk for overdose associated with ER/LA opioids might be particularly high during the first 2 weeks of treatment (KQ3). The contextual evidence review found that patients who do not have pain relief with opioids at 1 month are unlikely to experience pain relief with opioids at 6 months. Although evidence is insufficient to determine at what point within the first 3 months of opioid therapy the risks for opioid use disorder increase, reassessment of pain and function within 1 month of initiating opioids provides an opportunity to minimize risks of long-term opioid use by discontinuing opioids among patients not receiving a clear benefit from these medications. Experts noted that risks for opioid overdose are greatest during the first 3–7 days after opioid initiation or increase in dosage, particularly when methadone or transdermal fentanyl are prescribed; that follow-up within 3 days is appropriate when initiating or increasing the dosage of methadone; and that follow-up within 1 week might be appropriate when initiating or increasing the dosage of other ER/LA opioids.

Clinicians should evaluate patients to assess benefits and harms of opioids within 1 to 4 weeks of starting long-term opioid therapy or of dose escalation. Clinicians should consider follow-up intervals within the lower end of this range when ER/LA opioids are started or increased or when total daily opioid dosage is ≥50 MME/day. Shorter follow-up intervals (within 3 days) should be strongly considered when starting or increasing the dosage of methadone. At follow up, clinicians should assess benefits in function, pain control, and quality of life using tools such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) and/or asking patients about progress toward functional goals that have meaning for them (see Recommendation 2). Clinicians should also ask patients about common adverse effects such as constipation and drowsiness (see Recommendation 3), as well as asking about and assessing for effects that might be early warning signs for more serious problems such as overdose (e.g., sedation or slurred speech) or opioid use disorder (e.g., craving, wanting to take opioids in greater quantities or more frequently than prescribed, or difficulty controlling use). Clinicians should ask patients about their preferences for continuing opioids, given their effects on pain and function relative to any adverse effects experienced.

Because of potential changes in the balance of benefits and risks of opioid therapy over time, clinicians should regularly reassess all patients receiving long-term opioid therapy, including patients who are new to the clinician but on long-term opioid therapy, at least every 3 months. At reassessment, clinicians should determine whether opioids continue to meet treatment goals, including sustained improvement in pain and function, whether the patient has experienced common or serious adverse events or early warning signs of serious adverse events, signs of opioid use disorder (e.g., difficulty controlling use, work or family problems related to opioid use), whether benefits of opioids continue to outweigh risks, and whether opioid dosage can be reduced or opioids can be discontinued. Ideally, these reassessments would take place in person and be conducted by the prescribing clinician. In practice contexts where virtual visits are part of standard care (e.g., in remote areas where distance or other issues make follow-up visits challenging), follow-up assessments that allow the clinician to communicate with and observe the patient through video and audio could be conducted, with in-person visits occurring at least once per year. Clinicians should re-evaluate patients who are exposed to greater risk of opioid use disorder or overdose (e.g., patients with depression or other mental health conditions, a history of substance use disorder, a history of overdose, taking ≥50 MME/day, or taking other central nervous system depressants with opioids) more frequently than every 3 months. If clinically meaningful improvements in pain and function are not sustained, if patients are taking high-risk regimens (e.g., dosages ≥50 MME/day or opioids combined with benzodiazepines) without evidence of benefit, if patients believe benefits no longer outweigh risks or if they request dosage reduction or discontinuation, or if patients experience overdose or other serious adverse events (e.g., an event leading to hospitalization or disability) or warning signs of serious adverse events, clinicians should work with patients to reduce opioid dosage or to discontinue opioids when possible. Clinicians should maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to assist with pain management.

Considerations for Tapering Opioids

Although the clinical evidence review did not find high-quality studies comparing the effectiveness of different tapering protocols for use when opioid dosage is reduced or opioids are discontinued (KQ3), tapers reducing weekly dosage by 10%–50% of the original dosage have been recommended by other clinical guidelines (*199*), and a rapid taper over 2–3 weeks has been recommended in the case of a severe adverse event such as overdose (*30*). Experts noted that tapers slower than 10% per week (e.g., 10% per month) also might be appropriate and better tolerated than more rapid tapers, particularly when patients have been taking opioids for longer durations (e.g., for years). Opioid withdrawal during pregnancy has been associated with spontaneous abortion and premature labor.

When opioids are reduced or discontinued, a taper slow enough to minimize symptoms and signs of opioid withdrawal (e.g., drug craving, anxiety, insomnia, abdominal pain, vomiting, diarrhea, diaphoresis, mydriasis, tremor, tachycardia, or piloerection) should be used. A decrease of 10% of the original dose per week is a reasonable starting point; experts agreed that tapering plans may be individualized based on patient goals and concerns. Experts noted that at times, tapers might have to be paused and restarted again when the patient is ready and might have to be slowed once patients reach low dosages. Tapers may be considered successful as long as the patient is making progress. Once the smallest available dose is reached, the interval between doses can be extended. Opioids may be stopped when taken less frequently than once a day. More rapid tapers might be needed for patient safety under certain circumstances (e.g., for patients who have experienced overdose on their current dosage). Ultrarapid detoxification under anesthesia is associated with substantial risks, including death, and should not be used (*200*). Clinicians should access appropriate expertise if considering tapering opioids during pregnancy because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal. Patients who are not taking opioids (including patients who are diverting all opioids they obtain) do not require tapers. Clinicians should discuss with patients undergoing tapering the increased risk for overdose on abrupt return to a previously prescribed higher dose. Primary care clinicians should collaborate with mental health providers and with other specialists as needed to optimize nonopioid pain management (see Recommendation 1), as well as psychosocial support for anxiety related to the taper. More detailed guidance on tapering, including management of withdrawal symptoms has been published previously (*30*,*201*). If a patient exhibits signs of opioid use disorder, clinicians should offer or arrange for treatment of opioid use disorder (see Recommendation 12) and consider offering naloxone for overdose prevention (see Recommendation 8).

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present (recommendation category: A, evidence type: 4).

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on patient demographics or patient comorbidities (KQ2). However, based on the contextual evidence review and expert opinion, certain risk factors are likely to increase susceptibility to opioid-associated harms and warrant incorporation of additional strategies into the management plan to mitigate risk. Clinicians should assess these risk factors periodically, with frequency varying by risk factor and patient characteristics. For example, factors that vary more frequently over time, such as alcohol use, require more frequent follow up. In addition, clinicians should consider offering naloxone, re-evaluating patients more frequently (see Recommendation 7), and referring to pain and/or behavioral health specialists when factors that increase risk for harm, such as history of overdose, history of substance use disorder, higher dosages of opioids (≥50 MME/day), and concurrent use of benzodiazepines with opioids, are present.

Patients with Sleep-Disordered Breathing, Including Sleep Apnea

Risk factors for sleep-disordered breathing include congestive heart failure, and obesity. Experts noted that careful monitoring and cautious dose titration should be used if opioids are prescribed for patients with mild sleep-disordered breathing. Clinicians should avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing whenever possible to minimize risks for opioid overdose (contextual evidence review).

Pregnant Women

Opioids used in pregnancy might be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with stillbirth, poor fetal growth, pre-term delivery, and birth defects (contextual evidence review). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome. Clinicians and patients together should carefully weigh risks and benefits when making decisions

about whether to initiate opioid therapy for chronic pain during pregnancy. In addition, before initiating opioid therapy for chronic pain for reproductive-age women, clinicians should discuss family planning and how long-term opioid use might affect any future pregnancy. For pregnant women already receiving opioids, clinicians should access appropriate expertise if considering tapering opioids because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal (see Recommendation 7). For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine or methadone has been associated with improved maternal outcomes and should be offered (*202*) (see Recommendation 12). Clinicians caring for pregnant women receiving opioids for pain or receiving buprenorphine or methadone for opioid use disorder should arrange for delivery at a facility prepared to monitor, evaluate for, and treat neonatal opioid withdrawal syndrome. In instances when travel to such a facility would present an undue burden on the pregnant woman, it is appropriate to deliver locally, monitor and evaluate the newborn for neonatal opioid withdrawal syndrome, and transfer the newborn for additional treatment if needed. Neonatal toxicity and death have been reported in breast-feeding infants whose mothers are taking codeine (contextual evidence review); previous guidelines have recommended that codeine be avoided whenever possible among mothers who are breast feeding and, if used, should be limited to the lowest possible dose and to a 4-day supply (*203*).

Patients with Renal or Hepatic Insufficiency

Clinicians should use additional caution and increased monitoring (see Recommendation 7) to minimize risks of opioids prescribed for patients with renal or hepatic insufficiency, given their decreased ability to process and excrete drugs, susceptibility to accumulation of opioids, and reduced therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review; see Recommendations 4, 5, and 7).

Patients Aged ≥65 Years

Inadequate pain treatment among persons aged ≥65 years has been documented (*204*). Pain management for older patients can be challenging given increased risks of both nonopioid pharmacologic therapies (see Recommendation 1) and opioid therapy in this population. Given reduced renal function and medication clearance even in the absence of renal disease, patients aged ≥65 years might have increased susceptibility to accumulation of opioids and a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review). Some older adults suffer from cognitive impairment, which can increase risk for medication errors and make opioid-related confusion more dangerous. In addition, older adults are more likely than younger adults to experience co-morbid medical conditions and more likely to receive multiple medications, some of which might interact with opioids (such as benzodiazepines). Clinicians should use additional caution and increased monitoring (see Recommendations 4, 5, and 7) to minimize risks of opioids prescribed for patients aged ≥65 years. Experts suggested that clinicians educate older adults receiving opioids to avoid risky medication-related behaviors such as obtaining controlled medications from multiple prescribers and saving unused medications. Clinicians should also implement interventions to mitigate common risks of opioid therapy among older adults, such as exercise or bowel regimens to prevent constipation, risk assessment for falls, and patient monitoring for cognitive impairment.

Patients with Mental Health Conditions

Because psychological distress frequently interferes with improvement of pain and function in patients with chronic pain, using validated instruments such as the Generalized Anxiety Disorder (GAD)-7 and the Patient Health Questionnaire (PHQ)-9 or the PHQ-4 to assess for anxiety, post-traumatic stress disorder, and/or depression (*205*), might help clinicians improve overall pain treatment outcomes. Experts noted that clinicians should use additional caution and increased monitoring (see Recommendation 7) to lessen the increased risk for opioid use disorder among patients with mental health conditions (including depression, anxiety disorders, and PTSD), as well as increased risk for drug overdose among patients with depression. Previous guidelines have noted that opioid therapy should not be initiated during acute psychiatric instability or uncontrolled suicide risk, and that clinicians should consider behavioral health specialist consultation for any patient with a history of suicide attempt or psychiatric disorder (*31*). In addition, patients with anxiety disorders and other mental health conditions are more likely to receive benzodiazepines, which can exacerbate opioid-induced respiratory depression and increase risk for overdose (see Recommendation 11). Clinicians should ensure that treatment for depression and other mental health conditions is optimized, consulting with behavioral health specialists when needed. Treatment for depression can improve pain symptoms as well as depression and might decrease overdose risk (contextual evidence review). For treatment of chronic pain in patients with depression, clinicians should strongly consider using tricyclic or SNRI antidepressants for analgesic as well as antidepressant effects if these medications are not otherwise contraindicated (see Recommendation 1).

Patients with Substance Use Disorder

Illicit drugs and alcohol are listed as contributory factors on a substantial proportion of death certificates for opioid-related overdose deaths (contextual evidence review). Previous guidelines have recommended screening or risk assessment tools to identify patients at higher risk for misuse or abuse of opioids. However, the clinical evidence review found that currently available risk-stratification tools (e.g., Opioid Risk Tool, Screener and Opioid Assessment for Patients with Pain Version 1, SOAPP-R, and Brief Risk Interview) show insufficient accuracy for classification of patients as at low or high risk for abuse or misuse (KQ4). Clinicians should always exercise caution when considering or prescribing opioids for any patient with chronic pain outside of active cancer, palliative, and end-of-life care and should not overestimate the ability of these tools to rule out risks from long-term opioid therapy.

Clinicians should ask patients about their drug and alcohol use. Single screening questions can be used (*206*). For example, the question "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" (with an answer of one or more considered positive) was found in a primary care setting to be 100% sensitive and 73.5% specific for the detection of a drug use disorder compared with a standardized diagnostic interview (*207*). Validated screening tools such as the Drug Abuse Screening Test (DAST) (*208*) and the Alcohol Use Disorders Identification Test (AUDIT) (*209*) can also be used. Clinicians should use PDMP data (see Recommendation 9) and drug testing (see Recommendation 10) as appropriate to assess for concurrent substance use that might place patients at higher risk for opioid use disorder and overdose. Clinicians should also provide specific counseling on increased risks for overdose when opioids are combined with other drugs or alcohol (see Recommendation 3) and ensure that patients receive effective treatment for substance use disorders when needed (see Recommendation 12).

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on past or current substance use disorder (KQ2), although a history of substance use disorder was associated with misuse. Similarly, based on contextual evidence, patients with drug or alcohol use disorders are likely to experience greater risks for opioid use disorder and overdose than persons without these conditions. If clinicians consider opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care for patients with drug or alcohol use disorders, they should discuss increased risks for opioid use disorder and overdose with patients, carefully consider whether benefits of opioids outweigh increased risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed. Because pain management in patients with substance use disorder can be complex, clinicians should consider consulting substance use disorder specialists and pain specialists regarding pain management for persons with active or recent past history of substance abuse. Experts also noted that clinicians should communicate with patients' substance use disorder treatment providers if opioids are prescribed.

Patients with Prior Nonfatal Overdose

Although studies were not identified that directly addressed the risk for overdose among patients with prior nonfatal overdose who are prescribed opioids, based on clinical experience, experts thought that prior nonfatal overdose would substantially increase risk for future nonfatal or fatal opioid overdose. If patients experience nonfatal opioid overdose, clinicians should work with them to reduce opioid dosage and to discontinue opioids when possible (see Recommendation 7). If clinicians continue opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care in patients with prior opioid overdose, they should discuss increased risks for overdose with patients, carefully consider whether benefits of opioids outweigh substantial risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed.

Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present

Naloxone is an opioid antagonist that can reverse severe respiratory depression; its administration by lay persons, such as friends and family of persons who experience opioid overdose, can save lives. Naloxone precipitates acute withdrawal among patients physically dependent on opioids. Serious adverse effects, such as pulmonary edema, cardiovascular instability, and seizures, have been reported but are rare at doses consistent with labeled use for opioid overdose (*210*). The contextual evidence review did not find any studies on effectiveness of prescribing naloxone for overdose prevention among patients prescribed opioids for chronic pain. However, there is evidence for effectiveness of naloxone provision in preventing opioid-related overdose death at the community level through community-based distribution (e.g., through overdose education and naloxone distribution programs in community service agencies) to persons at risk for overdose

(mostly due to illicit opiate use), and it is plausible that effectiveness would be observed when naloxone is provided in the clinical setting as well. Experts agreed that it is preferable not to initiate opioid treatment when factors that increase risk for opioid-related harms are present. Opinions diverged about the likelihood of naloxone being useful to patients and the circumstances under which it should be offered. However, most experts agreed that clinicians should consider offering naloxone when prescribing opioids to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients taking benzodiazepines with opioids (see Recommendation 11), patients at risk for returning to a high dose to which they are no longer tolerant (e.g., patients recently released from prison), and patients taking higher dosages of opioids (≥50 MME/day). Practices should provide education on overdose prevention and naloxone use to patients receiving naloxone prescriptions and to members of their households. Experts noted that naloxone co-prescribing can be facilitated by clinics or practices with resources to provide naloxone training and by collaborative practice models with pharmacists. Resources for prescribing naloxone in primary care settings can be found through Prescribe to Prevent at http://prescribetoprevent.org.

9. **Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months (recommendation category: A, evidence type: 4).**

PDMPs are state-based databases that collect information on controlled prescription drugs dispensed by pharmacies in most states and, in select states, by dispensing physicians as well. In addition, some clinicians employed by the federal government, including some clinicians in the Indian Health Care Delivery System, are not licensed in the states where they practice, and do not have access to PDMP data. Certain states require clinicians to review PDMP data prior to writing each opioid prescription (see state-level PDMP-related policies on the National Alliance for Model State Drug Laws website at http://www.namsdl.org/prescription-monitoring-programs.cfm). The clinical evidence review did not find studies evaluating the effectiveness of PDMPs on outcomes related to overdose, addiction, abuse, or misuse (KQ4). However, even though evidence is limited on the effectiveness of PDMP implementation at the state level on prescribing and mortality outcomes (*28*), the contextual evidence review found that most fatal overdoses were associated with patients receiving opioids from multiple prescribers and/or with patients receiving high total daily opioid dosages; information on both of these risk factors for overdose are available to prescribers in the PDMP. PDMP data also can be helpful when patient medication history is not otherwise available (e.g., for patients from other locales) and when patients transition care to a new clinician. The contextual evidence review also found that PDMP information could be used in a way that is harmful to patients. For example, it has been used to dismiss patients from clinician practices (*211*), which might adversely affect patient safety.

The contextual review found variation in state policies that affect timeliness of PDMP data (and therefore benefits of reviewing PDMP data) as well as time and workload for clinicians in accessing PDMP data. In states that permit delegating access to other members of the health care team, workload for prescribers can be reduced. These differences might result in a different balance of benefits to clinician workload in different states. Experts agreed that PDMPs are useful tools that should be consulted when starting a patient on opioid therapy and periodically during long-term opioid therapy. However, experts disagreed on how frequently clinicians should check the PDMP during long-term opioid therapy, given PDMP access issues and the lag time in reporting in some states. Most experts agreed that PDMP data should be reviewed every 3 months or more frequently during long-term opioid therapy. A minority of experts noted that, given the current burden of accessing PDMP data in some states and the lack of evidence surrounding the most effective interval for PDMP review to improve patient outcomes, annual review of PDMP data during long-term opioid therapy would be reasonable when factors that increase risk for opioid-related harms are not present.

Clinicians should review PDMP data for opioids and other controlled medications patients might have received from additional prescribers to determine whether a patient is receiving high total opioid dosages or dangerous combinations (e.g., opioids combined with benzodiazepines) that put him or her at high risk for overdose. Ideally, PDMP data should be reviewed before every opioid prescription. This is recommended in all states with well-functioning PDMPs and where PDMP access policies make this practicable (e.g., clinician and delegate access permitted), but it is not currently possible in states without functional PDMPs or in those that do not permit certain prescribers to access them. As vendors and practices facilitate integration of PDMP information into regular clinical workflow (e.g., data made available in electronic health records), clinicians' ease of access in reviewing PDMP data is expected to improve.

In addition, improved timeliness of PDMP data will improve their value in identifying patient risks.

If patients are found to have high opioid dosages, dangerous combinations of medications, or multiple controlled substance prescriptions written by different clinicians, several actions can be taken to augment clinicians' abilities to improve patient safety:

- Clinicians should discuss information from the PDMP with their patient and confirm that the patient is aware of the additional prescriptions. Occasionally, PDMP information can be incorrect (e.g., if the wrong name or birthdate has been entered, the patient uses a nickname or maiden name, or another person has used the patient's identity to obtain prescriptions).
- Clinicians should discuss safety concerns, including increased risk for respiratory depression and overdose, with patients found to be receiving opioids from more than one prescriber or receiving medications that increase risk when combined with opioids (e.g., benzodiazepines) and consider offering naloxone (see Recommendation 8).
- Clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. Clinicians should communicate with others managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care (see Recommendation 11).
- Clinicians should calculate the total MME/day for concurrent opioid prescriptions to help assess the patient's overdose risk (see Recommendation 5). If patients are found to be receiving high total daily dosages of opioids, clinicians should discuss their safety concerns with the patient, consider tapering to a safer dosage (see Recommendations 5 and 7), and consider offering naloxone (see Recommendation 8).
- Clinicians should discuss safety concerns with other clinicians who are prescribing controlled substances for their patient. Ideally clinicians should first discuss concerns with their patient and inform him or her that they plan to coordinate care with the patient's other prescribers to improve the patient's safety.
- Clinicians should consider the possibility of a substance use disorder and discuss concerns with their patient (see Recommendation 12).
- If clinicians suspect their patient might be sharing or selling opioids and not taking them, clinicians should consider urine drug testing to assist in determining whether opioids can be discontinued without causing withdrawal (see Recommendations 7 and 10). A negative drug test for prescribed opioids might indicate the patient is not taking prescribed opioids, although clinicians should consider other possible reasons for this test result (see Recommendation 10).

Experts agreed that clinicians should not dismiss patients from their practice on the basis of PDMP information. Doing so can adversely affect patient safety, could represent patient abandonment, and could result in missed opportunities to provide potentially lifesaving information (e.g., about risks of opioids and overdose prevention) and interventions (e.g., safer prescriptions, nonopioid pain treatment [see Recommendation 1], naloxone [see Recommendation 8], and effective treatment for substance use disorder [see Recommendation 12]).

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs (recommendation category: B, evidence type: 4).

Concurrent use of opioid pain medications with other opioid pain medications, benzodiazepines, or heroin can increase patients' risk for overdose. Urine drug tests can provide information about drug use that is not reported by the patient. In addition, urine drug tests can assist clinicians in identifying when patients are not taking opioids prescribed for them, which might in some cases indicate diversion or other clinically important issues such as difficulties with adverse effects. Urine drug tests do not provide accurate information about how much or what dose of opioids or other drugs a patient took. The clinical evidence review did not find studies evaluating the effectiveness of urine drug screening for risk mitigation during opioid prescribing for pain (KQ4). The contextual evidence review found that urine drug testing can provide useful information about patients assumed not to be using unreported drugs. Urine drug testing results can be subject to misinterpretation and might sometimes be associated with practices that might harm patients (e.g., stigmatization, inappropriate termination from care). Routine use of urine drug tests with standardized policies at the practice or clinic level might destigmatize their use. Although random drug testing also might destigmatize urine drug testing, experts thought that truly random testing was not feasible in clinical practice. Some clinics obtain a urine specimen at every visit, but only send it for testing on a random schedule. Experts noted that in addition to direct costs of urine drug testing, which often are not covered fully by insurance and can be a burden for patients, clinician time is needed to interpret, confirm, and communicate results.

Experts agreed that prior to starting opioids for chronic pain and periodically during opioid therapy, clinicians should

use urine drug testing to assess for prescribed opioids as well as other controlled substances and illicit drugs that increase risk for overdose when combined with opioids, including nonprescribed opioids, benzodiazepines, and heroin. There was some difference of opinion among experts as to whether this recommendation should apply to all patients, or whether this recommendation should entail individual decision making with different choices for different patients based on values, preferences, and clinical situations. While experts agreed that clinicians should use urine drug testing before initiating opioid therapy for chronic pain, they disagreed on how frequently urine drug testing should be conducted during long-term opioid therapy. Most experts agreed that urine drug testing at least annually for all patients was reasonable. Some experts noted that this interval might be too long in some cases and too short in others, and that the follow-up interval should be left to the discretion of the clinician. Previous guidelines have recommended more frequent urine drug testing in patients thought to be at higher risk for substance use disorder (*30*). However, experts thought that predicting risk prior to urine drug testing is challenging and that currently available tools do not allow clinicians to reliably identify patients who are at low risk for substance use disorder.

In most situations, initial urine drug testing can be performed with a relatively inexpensive immunoassay panel for commonly prescribed opioids and illicit drugs. Patients prescribed less commonly used opioids might require specific testing for those agents. The use of confirmatory testing adds substantial costs and should be based on the need to detect specific opioids that cannot be identified on standard immunoassays or on the presence of unexpected urine drug test results. Clinicians should be familiar with the drugs included in urine drug testing panels used in their practice and should understand how to interpret results for these drugs. For example, a positive "opiates" immunoassay detects morphine, which might reflect patient use of morphine, codeine, or heroin, but this immunoassay does not detect synthetic opioids (e.g., fentanyl or methadone) and might not detect semisynthetic opioids (e.g., oxycodone). However, many laboratories use an oxycodone immunoassay that detects oxycodone and oxymorphone. In some cases, positive results for specific opioids might reflect metabolites from opioids the patient is taking and might not mean the patient is taking the specific opioid for which the test was positive. For example, hydromorphone is a metabolite of hydrocodone, and oxymorphone is a metabolite of oxycodone. Detailed guidance on interpretation of urine drug test results, including which tests to order and expected results, drug detection time in urine, drug metabolism, and other considerations has been published previously (*30*). Clinicians should not test for substances for which results would not affect patient management or for which implications for patient management are unclear. For example, experts noted that there might be uncertainty about the clinical implications of a positive urine drug test for tetrahyrdocannabinol (THC). In addition, restricting confirmatory testing to situations and substances for which results can reasonably be expected to affect patient management can reduce costs of urine drug testing, given the substantial costs associated with confirmatory testing methods. Before ordering urine drug testing, clinicians should have a plan for responding to unexpected results. Clinicians should explain to patients that urine drug testing is intended to improve their safety and should also explain expected results (e.g., presence of prescribed medication and absence of drugs, including illicit drugs, not reported by the patient). Clinicians should ask patients about use of prescribed and other drugs and ask whether there might be unexpected results. This will provide an opportunity for patients to provide information about changes in their use of prescribed opioids or other drugs. Clinicians should discuss unexpected results with the local laboratory or toxicologist and with the patient. Discussion with patients prior to specific confirmatory testing can sometimes yield a candid explanation of why a particular substance is present or absent and obviate the need for expensive confirmatory testing on that visit. For example, a patient might explain that the test is negative for prescribed opioids because she felt opioids were no longer helping and discontinued them. If unexpected results are not explained, a confirmatory test using a method selective enough to differentiate specific opioids and metabolites (e.g., gas or liquid chromatography/mass spectrometry) might be warranted to clarify the situation.

Clinicians should use unexpected results to improve patient safety (e.g., change in pain management strategy [see Recommendation 1], tapering or discontinuation of opioids [see Recommendation 7], more frequent re-evaluation [see Recommendation 7], offering naloxone [see Recommendation 8], or referral for treatment for substance use disorder [see Recommendation 12], all as appropriate). If tests for prescribed opioids are repeatedly negative, confirming that the patient is not taking the prescribed opioid, clinicians can discontinue the prescription without a taper. Clinicians should not dismiss patients from care based on a urine drug test result because this could constitute patient abandonment and could have adverse consequences for patient safety, potentially including the patient obtaining opioids from alternative sources and the clinician missing opportunities to facilitate treatment for substance use disorder.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently

whenever possible (recommendation category: A, evidence type: 3).

Benzodiazepines and opioids both cause central nervous system depression and can decrease respiratory drive. Concurrent use is likely to put patients at greater risk for potentially fatal overdose. The clinical evidence review did not address risks of benzodiazepine co-prescription among patients prescribed opioids. However, the contextual evidence review found evidence in epidemiologic series of concurrent benzodiazepine use in large proportions of opioid-related overdose deaths, and a case-cohort study found concurrent benzodiazepine prescription with opioid prescription to be associated with a near quadrupling of risk for overdose death compared with opioid prescription alone (*212*). Experts agreed that although there are circumstances when it might be appropriate to prescribe opioids to a patient receiving benzodiazepines (e.g., severe acute pain in a patient taking long-term, stable low-dose benzodiazepine therapy), clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. In addition, given that other central nervous system depressants (e.g., muscle relaxants, hypnotics) can potentiate central nervous system depression associated with opioids, clinicians should consider whether benefits outweigh risks of concurrent use of these drugs. Clinicians should check the PDMP for concurrent controlled medications prescribed by other clinicians (see Recommendation 9) and should consider involving pharmacists and pain specialists as part of the management team when opioids are co-prescribed with other central nervous system depressants. Because of greater risks of benzodiazepine withdrawal relative to opioid withdrawal, and because tapering opioids can be associated with anxiety, when patients receiving both benzodiazepines and opioids require tapering to reduce risk for fatal respiratory depression, it might be safer and more practical to taper opioids first (see Recommendation 7). Clinicians should taper benzodiazepines gradually if discontinued because abrupt withdrawal can be associated with rebound anxiety, hallucinations, seizures, delirium tremens, and, in rare cases, death (contextual evidence review). A commonly used tapering schedule that has been used safely and with moderate success is a reduction of the benzodiazepine dose by 25% every 1–2 weeks (*213*,*214*). CBT increases tapering success rates and might be particularly helpful for patients struggling with a benzodiazepine taper (*213*). If benzodiazepines prescribed for anxiety are tapered or discontinued, or if patients receiving opioids require treatment for anxiety, evidence-based psychotherapies (e.g., CBT) and/or specific anti-depressants or other nonbenzodiazepine medications approved for anxiety should be offered. Experts emphasized that clinicians should communicate with mental health professionals managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (recommendation category: A, evidence type: 2).

Opioid use disorder (previously classified as opioid abuse or opioid dependence) is defined in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) as a problematic pattern of opioid use leading to clinically significant impairment or distress, manifested by at least two defined criteria occurring within a year (http://pcssmat.org/wp-content/uploads/2014/02/5B-DSM-5-Opioid-Use-Disorder-Diagnostic-Criteria.pdf) (*20*).

The clinical evidence review found prevalence of opioid dependence (using DSM-IV diagnosis criteria) in primary care settings among patients with chronic pain on opioid therapy to be 3%–26% (KQ2). As found in the contextual evidence review and supported by moderate quality evidence, opioid agonist or partial agonist treatment with methadone maintenance therapy or buprenorphine has been shown to be more effective in preventing relapse among patients with opioid use disorder (*151*–*153*). Some studies suggest that using behavioral therapies in combination with these treatments can reduce opioid misuse and increase retention during maintenance therapy and improve compliance after detoxification (*154*,*155*); behavioral therapies are also recommended by clinical practice guidelines (*215*). The cited studies primarily evaluated patients with a history of illicit opioid use, rather than prescription opioid use for chronic pain. Recent studies among patients with prescription opioid dependence (based on DSM-IV criteria) have found maintenance therapy with buprenorphine and buprenorphine-naloxone effective in preventing relapse (*216*,*217*). Treatment need in a community is often not met by capacity to provide buprenorphine or methadone maintenance therapy (*218*), and patient cost can be a barrier to buprenorphine treatment because insurance coverage of buprenorphine for opioid use disorder is often limited (*219*). Oral or long-acting injectable formulations of naltrexone can also be used as medication-assisted treatment for opioid use disorder in nonpregnant adults, particularly for highly motivated persons (*220*,*221*). Experts agreed that clinicians prescribing opioids should identify treatment resources for opioid use disorder in the community and should work together to ensure sufficient treatment capacity for opioid use disorder at the practice level.

If clinicians suspect opioid use disorder based on patient concerns or behaviors or on findings in prescription drug monitoring program data (see Recommendation 9) or from urine drug testing (see Recommendation 10), they should discuss their concern with their patient and provide an opportunity for the patient to disclose related concerns or problems. Clinicians should assess for the presence of opioid use disorder using DSM-5 criteria (*20*). Alternatively, clinicians can arrange for a substance use disorder treatment specialist to assess for the presence of opioid use disorder. For patients meeting criteria for opioid use disorder, clinicians should offer or arrange for patients to receive evidence-based treatment, usually medication-assisted treatment with buprenorphine or methadone maintenance therapy in combination with behavioral therapies. Oral or long-acting injectable naltrexone, a long-acting opioid antagonist, can also be used in non-pregnant adults. Naltrexone blocks the effects of opioids if they are used but requires adherence to daily oral therapy or monthly injections. For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine (without naloxone) or methadone has been associated with improved maternal outcomes and should be offered (see Recommendation 8). Clinicians should also consider offering naloxone for overdose prevention to patients with opioid use disorder (see Recommendation 8). For patients with problematic opioid use that does not meet criteria for opioid use disorder, experts noted that clinicians can offer to taper and discontinue opioids (see Recommendation 7). For patients who choose to but are unable to taper, clinicians may reassess for opioid use disorder and offer opioid agonist therapy if criteria are met.

Physicians not already certified to provide buprenorphine in an office-based setting can undergo training to receive a waiver from the Substance Abuse and Mental Health Services Administration (SAMHSA) that allows them to prescribe buprenorphine to treat patients with opioid use disorder. Physicians prescribing opioids in communities without sufficient treatment capacity for opioid use disorder should strongly consider obtaining this waiver. Information about qualifications and the process to obtain a waiver are available from SAMHSA (*222*). Clinicians do not need a waiver to offer naltrexone for opioid use disorder as part of their practice.

Additional guidance has been published previously (*215*) on induction, use, and monitoring of buprenorphine treatment (see Part 5) and naltrexone treatment (see Part 6) for opioid use disorder and on goals, components of, and types of effective psychosocial treatment that are recommended in conjunction with pharmacological treatment of opioid use disorder (see Part 7). Clinicians unable to provide treatment themselves should arrange for patients with opioid use disorder to receive care from a substance use disorder treatment specialist, such as an office-based buprenorphine or naltrexone treatment provider, or from an opioid treatment program certified by SAMHSA to provide supervised medication-assisted treatment for patients with opioid use disorder. Clinicians should assist patients in finding qualified treatment providers and should arrange for patients to follow up with these providers, as well as arranging for ongoing coordination of care. Clinicians should not dismiss patients from their practice because of a substance use disorder because this can adversely affect patient safety and could represent patient abandonment. Identification of substance use disorder represents an opportunity for a clinician to initiate potentially life-saving interventions, and it is important for the clinician to collaborate with the patient regarding their safety to increase the likelihood of successful treatment. In addition, although identification of an opioid use disorder can alter the expected benefits and risks of opioid therapy for pain, patients with co-occurring pain and substance use disorder require ongoing pain management that maximizes benefits relative to risks. Clinicians should continue to use nonpharmacologic and nonopioid pharmacologic pain treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to provide optimal pain management.

Resources to help with arranging for treatment include SAMHSA's buprenorphine physician locator (http://buprenorphine.samhsa.gov/bwns_locator); SAMHSA's Opioid Treatment Program Directory (http://dpt2.samhsa.gov/treatment/directory.aspx); SAMHSA's Provider Clinical Support System for Opioid Therapies (http://pcss-o.org), which offers extensive experience in the treatment of substance use disorders and specifically of opioid use disorder, as well as expertise on the interface of pain and opioid misuse; and SAMHSA's Provider's Clinical Support System for Medication-Assisted Treatment (http://pcssmat.org), which offers expert physician mentors to answer questions about assessment for and treatment of substance use disorders.

Conclusions and Future Directions

Clinical guidelines represent one strategy for improving prescribing practices and health outcomes. Efforts are required to disseminate the guideline and achieve widespread adoption and implementation of the recommendations in clinical settings. CDC will translate this guideline into user-friendly materials for distribution and use by health systems, medical professional societies, insurers, public health departments, health information technology developers, and clinicians and engage in dissemination efforts. CDC has provided a

checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025), additional resources such as fact sheets (http://www.cdc.gov/drugoverdose/prescribing/resources.html), and will provide a mobile application to guide clinicians in implementing the recommendations. CDC will also work with partners to support clinician education on pain management options, opioid therapy, and risk mitigation strategies (e.g., urine drug testing). Activities such as development of clinical decision support in electronic health records to assist clinicians' treatment decisions at the point of care; identification of mechanisms that insurers and pharmacy benefit plan managers can use to promote safer prescribing within plans; and development of clinical quality improvement measures and initiatives to improve prescribing and patient care within health systems have promise for increasing guideline adoption and improving practice. In addition, policy initiatives that address barriers to implementation of the guidelines, such as increasing accessibility of PDMP data within and across states, e-prescribing, and availability of clinicians who can offer medication-assisted treatment for opioid use disorder, are strategies to consider to enhance implementation of the recommended practices. CDC will work with federal partners and payers to evaluate strategies such as payment reform and health care delivery models that could improve patient health and safety. For example, strategies might include strengthened coverage for nonpharmacologic treatments, appropriate urine drug testing, and medication-assisted treatment; reimbursable time for patient counseling; and payment models that improve access to interdisciplinary, coordinated care.

As highlighted in the forthcoming report on the National Pain Strategy, an overarching federal effort that outlines a comprehensive population-level health strategy for addressing pain as a public health problem, clinical guidelines complement other strategies aimed at preventing illnesses and injuries that lead to pain. A draft of the National Pain Strategy has been published previously (*180*). These strategies include strengthening the evidence base for pain prevention and treatment strategies, reducing disparities in pain treatment, improving service delivery and reimbursement, supporting professional education and training, and providing public education. It is important that overall improvements be made in developing the workforce to address pain management in general, in addition to opioid prescribing specifically. This guideline also complements other federal efforts focused on addressing the opioid overdose epidemic including prescriber training and education, improving access to treatment for opioid use disorder, safe storage and disposal programs, utilization management mechanisms, naloxone distribution programs, law enforcement and supply reduction efforts, prescription drug monitoring program improvements, and support for community coalitions and state prevention programs.

This guideline provides recommendations that are based on the best available evidence that was interpreted and informed by expert opinion. The clinical scientific evidence informing the recommendations is low in quality. To inform future guideline development, more research is necessary to fill in critical evidence gaps. The evidence reviews forming the basis of this guideline clearly illustrate that there is much yet to be learned about the effectiveness, safety, and economic efficiency of long-term opioid therapy. As highlighted by an expert panel in a recent workshop sponsored by the National Institutes of Health on the role of opioid pain medications in the treatment of chronic pain, "evidence is insufficient for every clinical decision that a provider needs to make about the use of opioids for chronic pain" (*223*). The National Institutes of Health panel recommended that research is needed to improve our understanding of which types of pain, specific diseases, and patients are most likely to be associated with benefit and harm from opioid pain medications; evaluate multidisciplinary pain interventions; estimate cost-benefit; develop and validate tools for identification of patient risk and outcomes; assess the effectiveness and harms of opioid pain medications with alternative study designs; and investigate risk identification and mitigation strategies and their effects on patient and public health outcomes. It is also important to obtain data to inform the cost feasibility and cost-effectiveness of recommended actions, such as use of nonpharmacologic therapy and urine drug testing. Research that contributes to safer and more effective pain treatment can be implemented across public health entities and federal agencies (*4*). Additional research can inform the development of future guidelines for special populations that could not be adequately addressed in this guideline, such as children and adolescents, where evidence and guidance is needed but currently lacking. CDC is committed to working with partners to identify the highest priority research areas to build the evidence base. Yet, given that chronic pain is recognized as a significant public health problem, the risks associated with long-term opioid therapy, the availability of effective nonpharmacological and nonopioid pharmacologic treatment options for pain, and the potential for improvement in the quality of health care with the implementation of recommended practices, a guideline for prescribing is warranted with the evidence that is currently available. The balance between the benefits and the risks of long-term opioid therapy for chronic pain based on both clinical and contextual evidence is strong enough to support the issuance of category A recommendations in most cases.

CDC will revisit this guideline as new evidence becomes available to determine when evidence gaps have been sufficiently closed to warrant an update of the guideline. Until this research is conducted, clinical practice guidelines will have to be based on the best available evidence and expert opinion. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC is committed to evaluating the guideline to identify the impact of the recommendations on clinician and patient outcomes, both intended and unintended, and revising the recommendations in future updates when warranted.

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TABLE 1. Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Effectiveness and comparative effectiveness (KQ1)							
Effectiveness of long-term opioid therapy versus placebo or no opioid therapy for long-term (≥1 year) outcomes							
Pain, function, and quality of life	None	—[†]	—	—	Insufficient	—	No evidence
Harms and adverse events (KQ2)							
Risks of opioids versus placebo or no opioids on opioid abuse, addiction, and related outcomes; overdose; and other harms							
Abuse or addiction	1 cohort study (n = 568,640)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	One retrospective cohort study found long-term use of prescribed opioids associated with an increased risk of abuse or dependence diagnosis versus no opioid use (adjusted OR ranged from 14.9 to 122.5, depending on dose).
Abuse or addiction	10 uncontrolled studies (n = 3,780)	Very serious limitations	Very serious inconsistency	No imprecision	4	None identified	In primary care settings, prevalence of opioid abuse ranged from 0.6% to 8% and prevalence of dependence from 3% to 26%. In pain clinic settings, prevalence of misuse ranged from 8% to 16% and addiction from 2% to 14%. Prevalence of aberrant drug-related behaviors ranged from 6% to 37%.
Overdose	1 cohort study (n = 9,940)	Serious limitations	Unknown (1 study)	Serious imprecision	3	None identified	Current opioid use associated with increased risk of any overdose events (adjusted HR 5.2, 95% CI = 2.1–12) and serious overdose events (adjusted HR 8.4, 95% CI = 2.5–28) versus current nonuse.
Fractures	1 cohort study (n = 2,341) and 1 case–control study (n = 21,739 case patients)	Serious limitations	No inconsistency	No imprecision	3	None identified	Opioid use associated with increased risk of fracture in 1 cohort study (adjusted HR 1.28, 95% CI = 0.99–1.64) and 1 case-control study (adjusted OR 1.27, 95% CI = 1.21–1.33).
Myocardial infarction	1 cohort study (n = 426,124) and 1 case–control study (n = 11,693 case patients)	No limitations	No inconsistency	No imprecision	3	None identified	Current opioid use associated with increased risk of myocardial infarction versus nonuse (adjusted OR 1.28, 95% CI = 1.19–1.37 and incidence rate ratio 2.66, 95% CI = 2.30–3.08).
Endocrinologic harms	1 cross-sectional study (n = 11,327)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	Long-term opioid use associated with increased risk for use of medications for erectile dysfunction or testosterone replacement versus nonuse (adjusted OR 1.5, 95% CI = 1.1–1.9).
How do harms vary depending on the opioid dose used?							
Abuse or addiction	1 cohort study (n = 568,640)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	One retrospective cohort study found higher doses of long-term opioid therapy associated with increased risk of opioid abuse or dependence than lower doses. Compared to no opioid prescription, the adjusted odds ratios were 15 (95% CI = 10–21) for 1 to 36 MME/day, 29 (95 % CI = 20–41) for 36 to120 MME/day, and 122 (95 % CI = 73–205) for ≥120 MME/day.
Overdose	1 cohort study (n = 9,940) and 1 case–control study (n = 593 case patients in primary analysis)	Serious limitations	No inconsistency	No imprecision	3	Magnitude of effect, dose response relationship	Versus 1 to <20 MME/day, one cohort study found an adjusted HR for an overdose event of 1.44 (95% CI = 0.57–3.62) for 20 to <50 MME/day that increased to 8.87 (95% CI = 3.99–19.72) at ≥100 MME/day; one case-control study found an adjusted OR for an opioid-related death of 1.32 (95% CI = 0.94–1.84) for 20 to 49 MME/day that increased to 2.88 (95% CI = 1.79–4.63) at ≥200 MME/day.
Fractures	1 cohort study (n = 2,341)	Serious limitations	Unknown (1 study)	Serious imprecision	3	None identified	Risk of fracture increased from an adjusted HR of 1.20 (95% CI = 0.92–1.56) at 1 to <20 MME/day to 2.00 (95% CI = 1.24–3.24) at ≥50 MME/day; the trend was of borderline statistical significance.

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Myocardial infarction	1 cohort study (n = 426,124)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	Relative to a cumulative dose of 0 to 1,350 MME during a 90-day period, the incidence rate ratio for myocardial infarction for 1350 to <2700 MME was 1.21 (95% CI = 1.02–1.45), for 2,700 to <8,100 MME was 1.42 (95% CI = 1.21–1.67), for 8,100 to <18,000 MME was 1.89 (95% CI = 1.54–2.33), and for ≥18,000 MME was 1.73 (95% CI = 1.32–2.26).
Motor vehicle crash injuries	1 case–control study (n = 5,300 case patients)	No limitations	Unknown (1 study)	No imprecision	3	None identified	No association between opioid dose and risk of motor vehicle crash injuries even though opioid doses >20 MME/day were associated with increased odds of road trauma among drivers.
Endocrinologic harms	1 cross-sectional study (n = 11,327) New for update: 1 additional cross-sectional study (n=1,585)	Serious limitations	Consistent	No imprecision	3	None identified	Relative to 0 to <20 MME/day, the adjusted OR for ≥120 MME/day for use of medications for erectile dysfunction or testosterone replacement was 1.6 (95% CI = 1.0–2.4). One new cross-sectional study found higher-dose long-term opioid therapy associated with increased risk of androgen deficiency among men receiving immediate-release opioids (adjusted OR per 10 MME/day 1.16, 95% CI = 1.09–1.23), but the dose response was very weak among men receiving ER/LA opioids.
Dosing strategies (KQ3)							
Comparative effectiveness of different methods for initiating opioid therapy and titrating doses							
Pain	3 randomized trials (n = 93)	Serious limitations	Serious inconsistency	Very serious imprecision	4	None identified	Trials on effects of titration with immediate-release versus ER/LA opioids reported inconsistent results and had additional differences between treatment arms in dosing protocols (titrated versus fixed dosing) and doses of opioids used.
Overdose	New for update: 1 cohort study (n = 840,606)	Serious limitations	Unknown (1 study)	No imprecision	4	None identified	One new cross-sectional study found initiation of therapy with an ER/LA opioid associated with increased risk of overdose versus initiation with an immediate-release opioid (adjusted HR 2.33, 95% CI = 1.26–4.32).
Comparative effectiveness of different ER/LA opioids							
Pain and function	3 randomized trials (n = 1,850)	Serious limitations	No inconsistency	No imprecision	3	None identified	No differences
All-cause mortality	1 cohort study (n = 108,492) New for update: 1 cohort study (n = 38,756)	Serious limitations	Serious inconsistency	No imprecision	4	None identified	One cohort study found methadone to be associated with lower all-cause mortality risk than sustained-release morphine in a propensity-adjusted analysis (adjusted HR 0.56, 95% CI = 0.51–0.62) and one cohort study among Tennessee Medicaid patients found methadone to be associated with higher risk of all-cause mortality than sustained-release morphine (adjusted HR 1.46, 95% CI = 1.17–1.73).
Abuse and related outcomes	1 cohort study (n = 5,684)	Serious limitations	Unknown (1 study)	Serious imprecision	4	None identified	One cohort study found some differences between ER/LA opioids in rates of adverse outcomes related to abuse, but outcomes were nonspecific for opioid-related adverse events, precluding reliable conclusions.
ER/LA versus immediate-release opioids							
Endocrinologic harms	New for update: 1 cross-sectional study (n = 1,585)	Serious limitations	Unknown (1 study)	No imprecision	4	None identified	One cross-sectional study found ER/LA opioids associated with increased risk of androgen deficiency versus immediate-release opioids (adjusted OR 3.39, 95% CI = 2.39–4.77).

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Dose escalation versus dose maintenance or use of dose thresholds							
Pain, function, or withdrawal due to opioid misuse	1 randomized trial (n = 140)	Serious limitations	Unknown (1 study)	Very serious imprecision	3	None identified	No difference between more liberal dose escalation versus maintenance of current doses in pain, function, or risk of withdrawal due to opioid misuse, but there was limited separation in opioid doses between groups (52 versus 40 MME/day at the end of the trial).
Immediate-release versus ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled and continuous versus as-needed dosing of opioids; or opioid rotation versus maintenance of current therapy							
Pain, function, quality of life, and outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effects of decreasing or tapering opioid doses versus continuation of opioid therapy							
Pain and function	1 randomized trial (n = 10)	Very serious limitations	Unknown (1 study)	Very serious imprecision	4	None identified	Abrupt cessation of morphine was associated with increased pain and decreased function compared with continuation of morphine.
Comparative effectiveness of different tapering protocols and strategies							
Opioid abstinence	2 nonrandomized trials (n = 150)	Very serious limitations	No inconsistency	Very serious imprecision	4	None identified	No clear differences between different methods for opioid discontinuation or tapering in likelihood of opioid abstinence after 3–6 months
Risk assessment and risk mitigation strategies (KQ4)							
Diagnostic accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse among patients with chronic pain being considered for long-term opioid therapy							
Opioid risk tool	3 studies of diagnostic accuracy (n = 496) New for update: 2 studies of diagnostic accuracy (n = 320)	Serious limitations	Very serious inconsistency	Serious imprecision	4	None identified	Based on a cutoff score of >4 (or unspecified), five studies (two fair-quality, three poor-quality) reported sensitivity that ranged from 0.20 to 0.99 and specificity that ranged from 0.16 to 0.88.
Screener and Opioid Assessment for Patients with Pain, Version 1	2 studies of diagnostic accuracy (n = 203)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a cutoff score of ≥8, sensitivity was 0.68 and specificity was 0.38 in one study, for a positive likelihood ratio of 1.11 and a negative likelihood ratio of 0.83. Based on a cutoff score of >6, sensitivity was 0.73 in one study.
Screener and Opioid Assessment for Patients with Pain-Revised	New for update: 2 studies of diagnostic accuracy (n = 320)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a cutoff score of >3 or unspecified, sensitivity was 0.25 and 0.53 and specificity was 0.62 and 0.73 in two studies, for likelihood ratios close to 1.
Brief Risk Interview	New for update: 2 studies of diagnostic accuracy (n = 320)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a "high risk" assessment, sensitivity was 0.73 and 0.83 and specificity was 0.43 and 0.88 in two studies, for positive likelihood ratios of 1.28 and 7.18 and negative likelihood ratios of 0.63 and 0.19.

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Comparative effectiveness of treatment strategies for managing patients with addiction to prescription opioids							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effects of opioid therapy for acute pain on long-term use (KQ5)							
Long-term opioid use	New for update: 2 cohort studies (n = 399,852)	Serious limitations	No inconsistency	No imprecision	3	None identified	One study found use of opioids within 7 days of low-risk surgery associated with increased likelihood of opioid use at 1 year (adjusted OR 1.44, 95% CI = 1.39–1.50), and one study found use of opioids within 15 days of onset of low back pain among workers with a compensation claim associated with increased risk of late opioid use (adjusted OR 2.08, 95% CI = 1.55–2.78 for 1 to 140 MME/day and OR 6.14, 95% CI = 4.92–7.66 for ≥450 MME/day).

Abbreviations: CI = confidence interval; ER/LA = extended release/long-acting; HR = hazard ratio; MME = morphine milligram equivalents; OR = odds ratio.
* Ratings were made per GRADE quality assessment criteria; "no limitations" indicates that limitations assessed through the GRADE method were not identified.
† Not applicable as no evidence was available for rating.

TABLE 2. Morphine milligram equivalent (MME) doses for commonly prescribed opioids

Opioid	Conversion factor*
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1–20 mg/day	4
21–40 mg/day	8
41–60 mg/day	10
≥61–80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3
Tapentadol†	0.4

Source: Adapted from Von Korff M, Saunders K, Ray GT, et al. Clin J Pain 2008;24:521–7 and Washington State Interagency Guideline on Prescribing Opioids for Pain (http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf).

* Multiply the dose for each opioid by the conversion factor to determine the dose in MMEs. For example, tablets containing hydrocodone 5 mg and acetaminophen 300 mg taken four times a day would contain a total of 20 mg of hydrocodone daily, equivalent to 20 MME daily; extended-release tablets containing oxycodone 10mg and taken twice a day would contain a total of 20mg of oxycodone daily, equivalent to 30 MME daily. The following cautions should be noted: 1) All doses are in mg/day except for fentanyl, which is mcg/hr. 2) Equianalgesic dose conversions are only estimates and cannot account for individual variability in genetics and pharmacokinetics. 3) Do not use the calculated dose in MMEs to determine the doses to use when converting opioid to another; when converting opioids the new opioid is typically dosed at substantially lower than the calculated MME dose to avoid accidental overdose due to incomplete cross-tolerance and individual variability in opioid pharmacokinetics. 4) Use particular caution with methadone dose conversions because the conversion factor increases at higher doses. 5) Use particular caution with fentanyl since it is dosed in mcg/hr instead of mg/day, and its absorption is affected by heat and other factors.

† Tapentadol is a mu receptor agonist and norepinephrine reuptake inhibitor. MMEs are based on degree of mu-receptor agonist activity, but it is unknown if this drug is associated with overdose in the same dose-dependent manner as observed with medications that are solely mu receptor agonists.

Steering Committee and Core Expert Group Members

Steering Committee: *Deborah Dowell, MD, Tamara M. Haegerich, PhD; Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC; Roger Chou, MD; on detail to CDC under contract.*

Core Expert Group Members: *Pam Archer, MPH, Oklahoma State Department of Health; Jane Ballantyne, MD; University of Washington (retired); Amy Bohnert, PhD; University of Michigan; Bonnie Burman, ScD; Ohio Department on Aging; Roger Chou, MD; on detail to CDC under contract; Phillip Coffin, MD, San Francisco Department of Public Health; Gary Franklin, MD, MPH; Washington State Department of Labor and Industries/University of Washington; Erin Krebs, MDH; Minneapolis VA Health Care System/University of Minnesota; Mitchel Mutter, MD, Tennessee Department of Health; Lewis Nelson, MD; New York University School of Medicine; Trupti Patel, MD, Arizona Department of Health Services; Christina A. Porucznik, PhD, University of Utah; Robert "Chuck" Rich, MD, FAAFP, American Academy of Family Physicians; Joanna Starrels, MD, Albert Einstein College of Medicine of Yeshiva University; Michael Steinman, MD, Society of General Internal Medicine; Thomas Tape, MD, American College of Physicians; Judith Turner, PhD, University of Washington.*

Stakeholder Review Group

John Markman, MD, American Academy of Neurology; Bob Twillman, PhD, American Academy of Pain Management; Edward C. Covington, MD, American Academy of Pain Medicine; Roger F. Suchyta, MD, FAAP, American Academy of Pediatrics; Kavitha V. Neerukonda, JD, American Academy of Physical Medicine and Rehabilitation; Mark Fleury, PhD, American Cancer Society Cancer Action Network; Penney Cowan, American Chronic Pain Association; David Juurlink, BPharm, MD, PhD, American College of Medical Toxicology; Gerald "Jerry" F. Joseph, Jr, MD, American College of Obstetrics and Gynecology; Bruce Ferrell, MD, AGSF, M. Carrington Reid, MD, PhD, American Geriatrics Society; Ashley Thompson, American Hospital Association; Barry D. Dickinson, PhD, American Medical Association; Gregory Terman MD, PhD, American Pain Society; Beth Haynes, MPPA, American Society of Addiction Medicine; Asokumar Buvanendran, MD, American Society of Anesthesiologists; Robert M. Plovnick; MD, American Society of Hematology; Sanford M. Silverman, MD, American Society of Interventional Pain Physicians; Andrew Kolodny, MD, Physicians for Responsible Opioid Prescribing.

Opioid Guideline Workgroup

Chair: *Christina Porucznik, PhD, MSPH*

Workgroup Members: *Anne Burns, RPh; Penney Cowan; Chinazo Cunningham, MD, MS; Katherine Galluzzi, DO; Traci Green, PhD, MSC; Mitchell Katz, MD; Erin Krebs, MD, MPH; Gregory Terman, MD, PhD; Mark Wallace, MD. Workgroup Consultants: Roger Chou, MD; Edward Covington, MD; Diana Eppolito; Michael Greene, MD; Steven Stanos, DO.*

Peer Reviewers

Jeanmarie Perrone, MD, University of Pennsylvania; Matthew Bair, MD, Indiana University School of Medicine;, David Tauben, MD, University of Washington.

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Errata

Vol. 65, No. RR-1

In the report, "CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016," three errors occurred. On page 1, the last sentence of the Summary should read, "CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025) as well as a website (**http://www.cdc.gov/drugoverdose/prescribing/resources.html**) with additional tools to guide clinicians in implementing the recommendations." On page 8, the first sentence of the first full paragraph should read, "NCIPC announced an open meeting of the NCIPC BSC in the Federal Register on January 11, **2016**." On page 49, in the fourth line of the Stakeholder Review Group, the affiliation for Gerald "Jerry" F. Joseph should read, "American College of **Obstetricians and Gynecologists**."

Vol. 65, No. 9

In the report, "Notes from the Field: Lymphocytic Choriomeningitis Virus Meningoencephalitis from a Household Rodent Infestation — Minnesota, 2015," on page 248, the first sentence of the fourth paragraph should read, "The family was referred for integrated pest management services through **the St. Paul-Ramsey County Department of Public Health, with assistance from the Minnesota Department of Health Healthy Homes grant program**."

THE PRESIDENT'S COMMISSION ON COMBATING DRUG ADDICTION AND THE OPIOID CRISIS

Roster of Commissioners

Governor Chris Christie, Chairman
Governor Charlie Baker
Governor Roy Cooper
Congressman Patrick J. Kennedy
Professor Bertha Madras, Ph.D.
Florida Attorney General Pam Bondi

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November 1, 2017

The Honorable Donald J. Trump
President of the United States
The White House
1600 Pennsylvania Avenue NW
Washington, DC 20500

Dear President Trump,

On behalf of the President's Commission on Combating Drug Addiction and the Opioid Crisis, we thank you for entrusting us with the responsibility of developing recommendations to combat the addiction crisis that is rampantly impacting our country.

Your speech in the East Room of the White House, along with the remarks of the First Lady, made it clear to the country that fighting this epidemic is a top priority of your Administration. On behalf of the Commission, we thank you for your leadership on this issue and on the clarity of your call to action.

When you declared the opioid crisis a national public health emergency under federal law on October 26, 2017, you acknowledged this crisis as one of epic proportion, impacting nearly every community across all 50 states. You signaled to the country that the force of the federal government should and will mobilize to reverse the rising tide of overdose deaths. You gave the millions of Americans fighting addiction hope that we can overcome this crisis, and we are prepared to win the fight.

Mr. President, as you acknowledged when you addressed the nation last week, the reason behind the urgent recommendations presented to you today by this Commission is that the leading cause of unintentional death in the United States is now drug overdose deaths.

Our people are dying. More than 175 lives lost every day. If a terrorist organization was killing 175 Americans a day on American soil, what would we do to stop them? We would do anything and everything. We must do the same to stop the dying caused from within. I know you will.

Without comprehensive action, including your national public health emergency, the death count will continue to rise. I know that is unacceptable to you. I know you will win this fight for the people who elected you.

You've met hundreds of parents who have buried their children, so these numbers are no longer simply statistics. Instead, they represent the injured student-athlete who becomes addicted after first prescription, ending her academic and athletic career, the newborn infant who is red and screaming from withdrawal pain, the grandparents using their retirement savings to raise young kids when the parents can't, the mom who just buried her only son, and the addict who cycles in and out of jail, simply because without access to treatment he is unable to stay sober and meet the terms of his parole.

It is time we all say what we know is true: addiction is a disease. However, we do not treat addiction in this country like we treat other diseases. Neither government nor the private sector has committed the support necessary for research, prevention, and treatment like we do for other diseases.

The recommendations herein, and the interim recommendations submitted by the Commission in July, are designed to address this national priority. These recommendations will help doctors, addiction treatment providers, parents, schools, patients, faith-based leaders, law enforcement, insurers, the medical industry, and researchers fight opioid abuse and misuse by reducing federal barriers and increasing support to effective programs and innovation.

Obviously, many of the recommendations that follow will require appropriations from Congress into the Public Health Emergency Fund, for block grants to states and to DOJ for enforcement and judicial improvements. It is not the Commission's charge to quantify the amount of these resources, so we do not do so in this report.

You have made fighting the opioid epidemic a national priority, Mr. President. And, the country is ready to follow your lead. Now, we urge Congress to do their constitutionally delegated duty and appropriate sufficient funds (as soon as possible) to implement the Commission's recommendations. 175 Americans are dying a day. Congress must act.

Here is what your Administration has already done:

- You acted to remove one of the biggest federal barriers to treatment by announcing the launch of a new policy to overcome the restrictive, decades-old federal rule that prevents states from providing more access to care at treatment facilities with more than 16 beds. This action will take people in crisis off waiting lists where they are at risk of losing their battle to their disease and put them into a treatment bed and on the path to recovery. We urge all Governors to apply to CMS for a waiver. This policy will – without any doubt – save lives. Governors across this nation thank you for listening to our call for help.
- In the interim report, the Commission also called for prescriber education and enhanced access to medication-assisted treatment for those already suffering from addiction. You acknowledged the need for these recommendations and directed all federally employed prescribers to receive special training to fight this epidemic. This is a bold step by you to deal with this issue.
- We recommended that the Department of Justice, which has already acted forcefully to stop the flow of illicit synthetic drugs into this country through the U.S. Postal Service, continue its efforts. The aggressive enforcement action being taken by your Administration is critical in our efforts to reduce the rise of overdose deaths in this country.

- National Institutes of Health (NIH) Director Dr. Francis Collins has been partnering with pharmaceutical companies to develop non-addictive painkillers and new treatments for addiction and overdose. The Commission worked with Dr. Collins to convene a meeting with industry leadership to discuss innovative ways to combat the opioid crisis. The Commission also held a public meeting to highlight the progress and innovation occurring today resulting from the NIH's work. This type of scientific progress is a positive step to help free the next generation from the widespread suffering addiction is causing today.

Our interim recommendations called for more data sharing among state-based prescription drug monitoring programs and recognized the need to address patient privacy regulations that make it difficult for health providers to access information and make informed healthcare decisions for someone who has a substance use disorder. We recommended that all law enforcement officers across the country be equipped with life-saving naloxone.

Finally, we recommended full enforcement of the Mental Health Parity and Addiction Equity Act to ensure that health plans cannot provide less favorable benefits for mental health and substance use diagnoses than physical health ailments. You will see further recommendations in our final report regarding the Parity Act and calling for the Department of Labor to have enhanced penalty and enforcement powers directly against insurers failing those who depend on them for life-saving treatment.

All the interim recommendations remain extremely relevant today and are critical tools to reduce ever increasing overdose deaths plaguing our citizens. The Commission is grateful the Administration has begun the hard work of implementing these initiatives. We urge you to implement the others as soon as possible.

Today, the Commission, as one its most urgent recommendations among the more than 50 provided in the final report, is calling for an expansive national multi-media campaign to fight this national health emergency.

This campaign, including aggressive television and social media outreach, must focus on telling our children of the dangers of these drugs and addiction, and on removing stigma as a barrier to treatment by emphasizing that addiction is not a moral failing, but rather a chronic brain disease with evidence-based treatment options. People need to be aware of the health risks associated with opioid use, and they must stop being afraid or ashamed of seeking help when facing their addiction.

Today, only 10.6% of youth and adults who need treatment for a substance use disorder receive that treatment. This is unacceptable. Too many people who could be helped are falling through the cracks and losing their lives as a result.

Many states, including my State of New Jersey, have undertaken this media strategy with significant positive results. However, having a nation-wide campaign will serve to reinforce the message and ensure, for example, that youth and young adults no longer believe that experimenting with pills from a doctor is safer than experimenting with illegal substances from a drug dealer.

As part of its prevention recommendations, the Commission also calls for better educating middle school, high school, and college students with the help of trained professionals such as nurses and counselors who can assess at-risk kids. Children have not escaped the consequences of

addiction and our efforts to reduce overdose deaths must start early. Mrs. Trump's dedication and leadership in helping our nation's children will make this a top priority and help save innocent young lives.

One of the most important recommendations in this final report is getting federal funding support more quickly and effectively to state governments, who are on the front lines of fighting this addiction battle every day. Bureaucracy, departmental silos, and red tape must not be accepted as the norm when dealing with funding to combat this epidemic. Saving time and resources, in this instance, will literally save lives.

Accordingly, we are urging Congress and the Administration to **block grant federal funding for opioid-related and SUD-related activities to the states**. There are multiple federal agencies and multiple grants within those agencies that cause states a significant administrative burden from an application and reporting perspective. Money is being wasted and accountability for results is not as intense as it should be. Block granting them would allow more resources to be spent on administering life-saving programs. This was a request to the Commission by nearly every Governor, regardless of party, across the country. And as a Commission that has three governors as members, all of whom know the frustration of jumping through multiple hoops to receive the funding we need to help our constituents in this fight, we wholeheartedly agree.

Throughout the comprehensive recommendations of its final report, the Commission also identifies the need to focus on, deploy and assess evidence-based programs that can be funded through these proposed block grants. Many of the recommendations acknowledge a need for better data analysis and accountability to ensure that any critical dollars are spent on what works best to fight this disease.

From its review of the federal budget aimed at addressing the opioid epidemic, the Commission identified a disturbing trend in federal health care reimbursement policies that incentivizes the wide-spread prescribing of opioids and limits access to other non-addictive treatments for pain, as well as addiction treatment and medication-assisted treatment.

First, individuals with acute or chronic pain must have access to non-opioid pain management options. Everything from physical therapy, to non-opioid medications, should be easily accessible as an alternative to opioids. The Commission heard from many innovative life sciences firms with new and promising products to treat patients' pain in non-addictive, safer ways; but they have trouble competing with cheap, generic opioids that are so widely used. We should incentivize insurers and the government to pay for non-opioid treatments for pain beginning right in the operating room and at every treatment step along the way.

In some cases, non-addictive pain medications are bundled in federal reimbursement policies so that hospitals and doctors are essentially not covered to prescribe non-opioid pain management alternatives. These types of policies, which the federal government can fix, are a significant deterrent to turning the tide on the health crisis we are facing. We urge you to order HHS to fix it.

Second, as a condition of full reimbursement of hospitals, CMS requires that hospitals randomly survey discharged patients. HHS previously included pain question response

information in calculations of incentive payment, but in 2017 thankfully abandoned this practice. However, all pain survey questions were not withdrawn from the surveys. The Commission recommends that CMS remove pain questions entirely when assessing consumers so that providers won't ever use opioids inappropriately to raise their survey scores. We urge you to order HHS to do this immediately.

The expectation of eliminating a patient's pain as an indication of successful treatment, and seeing pain as the fifth vital sign, which has been stated by some medical professionals as unique to the United States, was cited as a core cause of the culture of overprescribing in this country that led to the current health crisis. This must end immediately.

The Department of Labor must be given the real authority to regulate the health insurance industry. The health insurers are not following the federal law requiring parity in the reimbursement for mental health and addiction. They must be held responsible. The Secretary of Labor testified he needs the ability to fine violators and to individually investigate insurers not just employers. We agree with Secretary Acosta. If we do not get Congress to give him these tools, we will be failing our mission as badly as health insurance companies are failing their subscribers on this issue today leading to deaths.

Also contributing to this problem is the fact that HHS/CMS, the Indian Health Service, Tricare, and the VA still have reimbursement barriers to substance abuse treatment, including limiting access to certain FDA-approved medication-assisted treatment, counseling, and inpatient/residential treatment.

It's imperative that federal treatment providers lead the way to treating addiction as a disease and remove these barriers. Each of these primary care providers employed by the above-mentioned federal health systems should screen for SUDs and, directly or through referral, provide treatment within 24-to-48 hours. Each physician employee should be able to prescribe buprenorphine (if that is the most appropriate treatment for the patient) in primary care settings. As President, you can make this happen immediately. We urge you to do so.

A good example of this federal leadership occurred when Department of Veterans Affairs Secretary Shulkin, in response to the Commission's interim report release, immediately launched eight best practices for pain management in the VA health-care system. These guidelines included everything from alternatives and complimentary care, counseling and patient monitoring to peer education for front-line providers, informed consent of patients and naloxone distribution for Veterans on long-term opioid therapy. I had the opportunity to visit with doctors and patients at the Louis Stokes Northeast Ohio VA Healthcare System and witnessed first-hand the positive results of a hospital that has embraced a different continuum of care for pain management. The VA doctors, which included behavioral health specialists, acknowledge and treat those with addiction in the full complement of ways the medical community would tackle other chronic diseases. Let's use these VA practices as an example for our entire healthcare system.

As you will see in the Commission's recommendations, the Federal Government has a number of avenues through which it can ensure that individuals with addiction disorders get the help they need; including changing CMS reimbursement policies, enforcing parity laws against non-compliant insurers, promoting access to rural communities through such tools as telemedicine,

and incenting a larger treatment workforce to address the broad scope of the crisis.

For individuals with a substance use disorder, ensuring life-saving access to affordable health care benefits is an essential tool in fighting the opioid epidemic. Look at Indiana as an example. After Indiana used an insurance access program to rapidly respond to a rural, opioid-related health crisis, the Indiana Department of Health reported that such a program opened the door to life changing medical treatment.

We are recommending that a drug court be established in every one of the 93 federal district courts in America. It is working in our states and can work in our federal system to help treat those who need it and lower the federal prison population. For many people, being arrested and sent to a drug court is what saved their lives, allowed them to get treatment, and gave them a second chance.

Drug Courts are known to be significantly more effective than incarceration, but 44% of U.S. Counties do not have an adult drug court. DOJ should urge states to establish state drug courts in every county. When individuals violate the terms of probation or parole with substance use, they need to be diverted to drug court, rather than back to incarceration. Further, drug courts need to embrace the use of medication-assisted treatment for their populations, as it clearly improves outcomes. The criminal justice system should accept that medication, when clinically appropriate, can lead to lasting recovery; abstinence-only sobriety is not the only path to recovery.

Lastly, the Commission's recommendations identify multiple ways to reduce the supply of licit and illicit opioids and enhanced enforcement strategies. Recognizing the growing threat of synthetic opioids such as fentanyl, the Commission recommends enhanced penalties for trafficking of fentanyl and fentanyl analogues and calls for additional technologies and drug detection methods to expand efforts to intercept fentanyl before entering the country.

To help protect first responders, who are also on the front lines fighting this epidemic responding to overdoses sometimes multiple times a day, the Commission recommends the White House develop a national outreach strategy coordinating with Governors for the release and adoption of the Office of Homeland Security National Security Council's new *Fentanyl Safety Recommendations for First Responders*. The Commission thanks White House Homeland Security Advisor Tom Bossert for his support and hard work already on this initiative.

Many other thoughtful, vital recommendations are included herein. These recommendations were informed by expert testimony provided during the Commission's public meetings, which included treatment providers and experts, pharmaceutical innovators and insurers. They also were informed by thousands of written submissions accepted by the Commission as part of its public process.

The Commission acknowledges that there is an active movement to promote the use of marijuana as an alternative medication for chronic pain and as a treatment for opioid addiction. Recent research out of the NIH's National Institute on Drug Abuse found that marijuana use led to a 2 ½ times greater chance that the marijuana user would become an opioid user and abuser. The Commission found this very disturbing. There is a lack of sophisticated outcome data on dose, potency, drug-drug interactions, effectiveness, and long-term consequences of marijuana used for

medical purposes. This mirrors the lack of data in the 1990's and early 2000's when opioid prescribing multiplied across health care settings and led to the current epidemic of abuse, misuse and addiction. The Commission urges that the same mistake is not made with the uninformed rush to put another drug legally on the market in the midst of an overdose epidemic.

The Commission extends our sincere gratitude to all of the individuals, organizations, families, companies, state officials, federal agency staff, and clinical professionals who provided personal stories, creative solutions, and thoughtful input to the Commission. The Commission members received thousands of letters, took hundreds of phone calls and meetings, and heard testimony from prominent organizations including non-profits, professional societies, pharmaceutical companies, health insurance providers, and most importantly, individuals and families that have been in the throes of addiction. These letters, conversations, and meetings were the impetus for the vast majority of recommendations made in this report.

The Commission is confident that, if enacted quickly, these recommendations will strengthen the federal government, state, and local response to this crisis. But it will take all invested parties to step up and play a role: the federal executive branch, Congress, states, the pharmaceutical industry, doctors, pharmacists, academia, and insurers. The responsibility is all of ours. We must come together for the collective good and acknowledge that this disease requires a coordinated and comprehensive attack from all of us.

The time to wait is over. The time for talk is passed. 175 deaths a day can no longer be tolerated. We know that you will not stand by; we believe you will force action.

Along with my fellow Commission members, and the thousands of people who contributed to this report by sharing their stories and ideas for solutions, I look forward to seeing these policy changes implemented. Thank you again for the opportunity to serve, and most of all thank you for your commitment to addressing this vital national public health emergency.

Sincerely,

Governor Chris Christie
Governor of New Jersey
Chairman, President's Commission on Combating
Drug Addiction and the Opioid Crisis

Summary of Recommendations

Federal Funding and Programs

1. The Commission urges Congress and the Administration to block grant federal funding for opioid-related and SUD-related activities to the states, where the battle is happening every day. There are multiple federal agencies and multiple grants within those agencies that cause states a significant administrative burden from an application and reporting perspective. Creating uniform block grants would allow more resources to be spent on administering life-saving programs. This was a request to the Commission by nearly every Governor, regardless of party, across the country.

2. The Commission believes that ONDCP must establish a coordinated system for tracking all federally-funded initiatives, through support from HHS and DOJ. If we are to invest in combating this epidemic, we must invest in only those programs that achieve quantifiable goals and metrics. We are operating blindly today; ONDCP must establish a system of tracking and accountability.

3. To achieve accountability in federal programs, the Commission recommends that ONDCP review is a component of every federal program and that necessary funding is provided for implementation. Cooperation by federal agencies and the states must be mandated.

Opioid Addiction Prevention

4. The Commission recommends that Department of Education (DOE) collaborate with states on student assessment programs such as Screening, Brief Intervention and Referral to Treatment (SBIRT). SBIRT is a program that uses a screening tool by trained staff to identify at-risk youth who may need treatment. This should be deployed for adolescents in middle school, high school and college levels. This is a significant prevention tool.

5. The Commission recommends the Administration fund and collaborate with private sector and non-profit partners to design and implement a wide-reaching, national multi-platform media campaign addressing the hazards of substance use, the danger of opioids, and stigma. A similar mass media/educational campaign was launched during the AIDs public health crisis.

Prescribing Guidelines, Regulations, Education

6. The Commission recommends HHS, the Department of Labor (DOL), VA/DOD, FDA, and ONDCP work with stakeholders to develop model statutes, regulations, and policies that ensure informed patient consent prior to an opioid prescription for chronic pain. Patients need to understand the risks, benefits and alternatives to taking opioids. This is not the standard today.

7. The Commission recommends that HHS coordinate the development of a national curriculum and standard of care for opioid prescribers. An updated set of guidelines for prescription pain medications should be established by an expert committee composed of various specialty

practices to supplement the CDC guideline that are specifically targeted to primary care physicians.

8. The Commission recommends that federal agencies work to collect participation data. Data on prescribing patterns should be matched with participation in continuing medical education data to determine program effectiveness and such analytics shared with clinicians and stakeholders such as state licensing boards.

9. The Commission recommends that the Administration develop a model training program to be disseminated to all levels of medical education (including all prescribers) on screening for substance use and mental health status to identify at risk patients.

10. The Commission recommends the Administration work with Congress to amend the Controlled Substances Act to allow the DEA to require that all prescribers desiring to be relicensed to prescribe opioids show participation in an approved continuing medical education program on opioid prescribing.

11. The Commission recommends that HHS, DOJ/DEA, ONDCP, and pharmacy associations train pharmacists on best practices to evaluate legitimacy of opioid prescriptions, and not penalize pharmacists for denying inappropriate prescriptions.

PDMP Enhancements

12. The Commission recommends the Administration's support of the Prescription Drug Monitoring (PDMP) Act to mandate states that receive grant funds to comply with PDMP requirements, including data sharing. This Act directs DOJ to fund the establishment and maintenance of a data-sharing hub.

13. The Commission recommends federal agencies mandate PDMP checks, and consider amending requirements under the Emergency Medical Treatment and Labor Act (EMTALA), which requires hospitals to screen and stabilize patients in an emergency department, regardless of insurance status or ability to pay.

14. The Commission recommends that PDMP data integration with electronic health records, overdose episodes, and SUD-related decision support tools for providers is necessary to increase effectiveness.

15. The Commission recommends ONDCP and DEA increase electronic prescribing to prevent diversion and forgery. The DEA should revise regulations regarding electronic prescribing for controlled substances.

16. The Commission recommends that the Federal Government work with states to remove legal barriers and ensure PDMPs incorporate available overdose/naloxone deployment data, including the Department of Transportation’s (DOT) Emergency Medical Technician (EMT) overdose database. It is necessary to have overdose data/naloxone deployment data in the PDMP to allow users of the PDMP to assist patients.

Supply Reduction and Enforcement Strategies

17. The Commission recommends community-based stakeholders utilize Take Back Day to inform the public about drug screening and treatment services. The Commission encourages more hospitals/clinics and retail pharmacies to become year-round authorized collectors and explore the use of drug deactivation bags.

18. The Commission recommends that CMS remove pain survey questions entirely on patient satisfaction surveys, so that providers are never incentivized for offering opioids to raise their survey score. ONDCP and HHS should establish a policy to prevent hospital administrators from using patient ratings from CMS surveys improperly.

19. The Commission recommends CMS review and modify rate-setting policies that discourage the use of non-opioid treatments for pain, such as certain bundled payments that make alternative treatment options cost prohibitive for hospitals and doctors, particularly those options for treating immediate post-surgical pain.

20. The Commission recommends a federal effort to strengthen data collection activities enabling real-time surveillance of the opioid crisis at the national, state, local, and tribal levels.

21. The Commission recommends the Federal Government work with the states to develop and implement standardized rigorous drug testing procedures, forensic methods, and use of appropriate toxicology instrumentation in the investigation of drug-related deaths. We do not have sufficiently accurate and systematic data from medical examiners around the country to determine overdose deaths, both in their cause and the actual number of deaths.

22. The Commission recommends reinstituting the *Arrestee Drug Abuse Monitoring* (ADAM) program and the *Drug Abuse Warning Network* (DAWN) to improve data collection and provide resources for other promising surveillance systems.

23. The Commission recommends the enhancement of federal sentencing penalties for the trafficking of fentanyl and fentanyl analogues.

24. The Commission recommends that federal law enforcement agencies expressly target Drug Trafficking Organizations and other individuals who produce and sell counterfeit pills, including through the internet.

25. The Commission recommends that the Administration work with Congress to amend the law to give the DEA the authority to regulate the use of pill presses/tableting machines with requirements for the maintenance of records, inspections for verifying location and stated use, and security provisions.

26. The Commission recommends U.S. Customs and Border Protection (CBP) and the U.S. Postal Inspection Service (USPIS) use additional technologies and drug detection canines to expand efforts to intercept fentanyl (and other synthetic opioids) in envelopes and packages at international mail processing distribution centers.

27. The Commission recommends Congress and the Federal Government use advanced electronic data on international shipments from high-risk areas to identify international suppliers and their U.S.-based distributors.

28. The Commission recommends support of the Synthetics Trafficking and Overdose Prevention (STOP) Act and recommends the Federal Government work with the international community to implement the STOP Act in accordance with international laws and treaties.

29. The Commission recommends a coordinated federal/DEA effort to prevent, monitor and detect the diversion of prescription opioids, including licit fentanyl, for illicit distribution or use.

30. The Commission recommends the White House develop a national outreach plan for the *Fentanyl Safety Recommendations for First Responders*. Federal departments and agencies should partner with Governors and state fusion centers to develop and standardize data collection, analytics, and information-sharing related to first responder opioid-intoxication incidents.

Opioid Addiction Treatment, Overdose Reversal, and Recovery

31. The Commission recommends HHS, CMS, Substance Abuse and Mental Health Services Administration, the VA, and other federal agencies incorporate quality measures that address addiction screenings and treatment referrals. There is a great need to ensure that health care providers are screening for SUDs and know how to appropriately counsel, or refer a patient. HHS should review the scientific evidence on the latest OUD and SUD treatment options and collaborate with the U.S. Preventive Services Task Force (USPSTF) on provider recommendations.

32. The Commission recommends the adoption of process, outcome, and prognostic measures of treatment services as presented by the National Outcome Measurement and the American Society of Addiction Medicine (ASAM). Addiction is a chronic relapsing disease of the brain which affects multiple aspects of a person's life. Providers, practitioners, and funders often face challenges in helping individuals achieve positive long-term outcomes without relapse.

33. The Commission recommends HHS/CMS, the Indian Health Service (IHS), Tricare, the DEA, and the VA remove reimbursement and policy barriers to SUD treatment, including those, such as patient limits, that limit access to any forms of FDA-approved medication-assisted treatment (MAT), counseling, inpatient/residential treatment, and other treatment modalities, particularly fail-first protocols and frequent prior authorizations. All primary care providers employed by the above-mentioned health systems should screen for alcohol and drug use and, directly or through referral, provide treatment within 24 to 48 hours.

34. The Commission recommends HHS review and modify rate-setting (including policies that indirectly impact reimbursement) to better cover the true costs of providing SUD treatment, including inpatient psychiatric facility rates and outpatient provider rates.

35. Because the Department of Labor (DOL) regulates health care coverage provided by many large employers, the Commission recommends that Congress provide DOL increased authority to levy monetary penalties on insurers and funders, and permit DOL to launch investigations of health insurers independently for parity violations.

36. The Commission recommends that federal and state regulators should use a standardized tool that requires health plans to document and disclose their compliance strategies for non-quantitative treatment limitations (NQTL) parity. NQTLs include stringent prior authorization

and medical necessity requirements. HHS, in consultation with DOL and Treasury, should review clinical guidelines and standards to support NQTL parity requirements. Private sector insurers, including employers, should review rate-setting strategies and revise rates when necessary to increase their network of addiction treatment professionals.

37. The Commission recommends the National Institute on Corrections (NIC), the Bureau of Justice Assistance (BJA), the Substance Abuse and Mental Health Services Administration (SAMHSA), and other national, state, local, and tribal stakeholders use medication-assisted treatment (MAT) with pre-trial detainees and continuing treatment upon release.

38. The Commission recommends DOJ broadly establish federal drug courts within the federal district court system in all 93 federal judicial districts. States, local units of government, and Indian tribal governments should apply for drug court grants established by 34 U.S.C. § 10611. Individuals with an SUD who violate probation terms with substance use should be diverted into drug court, rather than prison.

39. The Commission recommends the Federal Government partner with appropriate hospital and recovery organizations to expand the use of recovery coaches, especially in hard-hit areas. Insurance companies, federal health systems, and state payers should expand programs for hospital and primary case-based SUD treatment and referral services. Recovery coach programs have been extraordinarily effective in states that have them to help direct patients in crisis to appropriate treatment. Addiction and recovery specialists can also work with patients through technology and telemedicine, to expand their reach to underserved areas.

40. The Commission recommends the Health Resources and Services Administration (HRSA) prioritize addiction treatment knowledge across all health disciplines. Adequate resources are needed to recruit and increase the number of addiction-trained psychiatrists and other physicians, nurses, psychologists, social workers, physician assistants, and community health workers and facilitate deployment in needed regions and facilities.

41. The Commission recommends that federal agencies revise regulations and reimbursement policies to allow for SUD treatment via telemedicine.

42. The Commission recommends further use of the National Health Service Corp to supply needed health care workers to states and localities with higher than average opioid use and abuse.

43. The Commission recommends the National Highway Traffic Safety Administration (NHTSA) review its National Emergency Medical Services (EMS) Scope of Practice Model with respect to naloxone, and disseminate best practices for states that may need statutory or regulatory changes to allow Emergency Medical Technicians (EMT) to administer naloxone, including higher doses to account for the rising number of fentanyl overdoses.

44. The Commission recommends HHS implement naloxone co-prescribing pilot programs to confirm initial research and identify best practices. ONDCP should, in coordination with HHS, disseminate a summary of existing research on co-prescribing to stakeholders.

45. The Commission recommends HHS develop new guidance for Emergency Medical Treatment and Labor Act (EMTALA) compliance with regard to treating and stabilizing SUD patients and provide resources to incentivize hospitals to hire appropriate staff for their emergency rooms.

46. The Commission recommends that HHS implement guidelines and reimbursement policies for Recovery Support Services, including peer-to-peer programs, jobs and life skills training, supportive housing, and recovery housing.

47. The Commission recommends that HHS, the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Administration on Children, Youth and Families (ACYF) should disseminate best practices for states regarding interventions and strategies to keep families together, when it can be done safely (e.g., using a relative for kinship care). These practices should include utilizing comprehensive family centered approaches and should ensure families have access to drug screening, substance use treatment, and parental support. Further, federal agencies should research promising models for pregnant and post-partum women with SUDs and their newborns, including screenings, treatment interventions, supportive housing, non-pharmacologic interventions for children born with neonatal abstinence syndrome, medication-assisted treatment (MAT) and other recovery supports.

48. The Commission recommends ONDCP, the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Department of Education (DOE) identify successful college recovery programs, including "sober housing" on college campuses, and provide support and technical assistance to increase the number and capacity of high-quality programs to help students in recovery.

49. The Commission recommends that ONDCP, federal partners, including DOL, large employers, employee assistance programs, and recovery support organizations develop best practices on SUDs and the workplace. Employers need information for addressing employee alcohol and drug use, ensure that employees are able to seek help for SUDs through employee assistance programs or other means, supporting health and wellness, including SUD recovery, for employees, and hiring those in recovery.

50. The Commission recommends that ONDCP work with the DOJ, DOL, the National Alliance for Model State Drug Laws, the National Conference of State Legislatures, and other stakeholders to develop model state legislation/regulation for states to decouple felony convictions and eligibility for business/occupational licenses, where appropriate.

51. The Commission recommends that ONDCP, federal agencies, the National Alliance for Recovery Residents (NARR), the National Association of State Alcohol and Drug Abuse Directors (NASADAD), and housing stakeholders should work collaboratively to develop quality standards and best practices for recovery residences, including model state and local policies. These partners should identify barriers (such as zoning restrictions and discrimination against MAT patients) and develop strategies to address these issues.

Research and Development

52. The Commission recommends federal agencies, including HHS (National Institutes of Health, CDC, CMS, FDA, and the Substance Abuse and Mental Health Services Administration), DOJ, the Department of Defense (DOD), the VA, and ONDCP, should engage in a comprehensive review of existing research programs and establish goals for pain management and addiction research (both prevention and treatment).

53. The Commission recommends Congress and the Federal Government provide additional resources to the National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), and National Institute on Alcohol Abuse and Alcoholism (NIAAA) to fund the research areas cited above. NIDA should continue research in concert with the pharmaceutical industry to develop and test innovative medications for SUDs and OUDs, including long-acting injectables, more potent opioid antagonists to reverse overdose, drugs used for detoxification, and opioid vaccines.

54. The Commission recommends further research of Technology-Assisted Monitoring and Treatment for high-risk patients and SUD patients. CMS, FDA, and the United States Preventative Services Task Force (USPSTF) should implement a fast-track review process for any new evidence-based technology supporting SUD prevention and treatments.

55. The Commission recommends that commercial insurers and CMS fast-track creation of Healthcare Common Procedure Coding System (HCPCS) codes for FDA-approved technology-based treatments, digital interventions, and biomarker-based interventions. NIH should develop a means to evaluate behavior modification apps for effectiveness.

56. The Commission recommends that the FDA establish guidelines for post-market surveillance related to diversion, addiction, and other adverse consequences of controlled substances.

The Drug Addiction and Opioid Crisis

The primary goal of the President's Commission on Combating Drug Addiction and the Opioid Crisis is to develop an effective set of recommendations for the President to combat the opioid crisis and drug addiction in our nation. Many of the recommendations that follow will require appropriations from Congress into the Public Health Emergency Fund, for block grants to states and to DOJ for enforcement and judicial improvements. It is not the Commission's charge to quantify the amount of these resources, so we do not do so in this report.

The Commission urges Congress to respond to the President's declaration of a Public Health Emergency and fulfill their constitutionally delegated duty and appropriate sufficient funds to implement the Commission's recommendations. 175 Americans are dying every day. Congress must act. Notwithstanding this core mission, it is vital to address the influences that transformed the United States into the world leader of opioid prescribing, opioid addiction, and opioid overdose deaths.

Origins of the Current Crisis

The Current Crisis. In the mid- to late-19th century, the first national opioid crisis occurred; a detailed history is provided in Appendix 2. During this time, opioid use rose dramatically, fueled by physicians' unrestrained opioid prescriptions (morphine, laudanum, paregoric, codeine, and heroin) for pain or other ailments, and by liberal use of opioid-based treatments for injuries and diseases impacting Civil War combatants and veterans (see Appendix 2). In parallel with the current crisis, this nation-wide crisis extended across socio-economic statuses, and reached urban and rural areas. This first epidemic was eventually contained and reversed by physicians, pharmacists, medical education, and voluntary restraint, combined with federal regulations and law enforcement.

After the first crisis subsided, medical education emphasized the hazards of improper opioid prescribing, and by doing so, created a cultural mindset against the dangers of opioids. However, over 30 years ago, a sequence of events eroded fears of opioids, and the medical community once again relapsed into liberal use of medicinal opioids.

Triggered by excessive prescribing of opioids since 1999, the current crisis is being fueled by several factors that did not exist in the 19th century: the advent of large scale production and distribution of pure, potent, orally effective and addictive opioids; the widespread availability of inexpensive and purer illicit heroin; the influx of highly potent fentanyl/fentanyl analogs; the transition of prescription opioid misusers into use of heroin and fentanyl; and the production of illicit opioid pills containing deadly fentanyl(s) made by authentic pill presses. Prescription opioids now affect a wide age range, families both well-off and financially disadvantaged, urban and rural, and all ethnic and racial groups.

Historical precedent demonstrated that this crisis can be fought with effective medical education, voluntary or involuntary changes in prescribing practices, and a strong regulatory and enforcement environment. The recommendations of the Commission are grounded in this reality, and benefit from modern systematic epidemiological and large data analytics, evidence-based treatments, and medications to assist in recovery or rescue of an overdose crisis.

Contributors to the Current Crisis. A widely held and supportable view is that the modern opioid crisis originated within the healthcare system and have been influenced by several factors:

- **Unsubstantiated claims:** One early catalyst can be traced to a single letter to the Editor of the New England Journal of Medicine published in 1980, that was then cited by over 600 subsequent articles.[1,2] With the headline "Addiction Rare in Patients Treated with Narcotics," the flawed conclusion of the five-sentence letter was based on scrutiny of records of hospitalized patients administered an opioid. It offered no information on opioid dose, number of doses, the duration of opioid treatment, whether opioids were consumed after hospital discharge, or long-term follow-up, nor a description of criteria used to designate opioid addiction. Six years later, another problematic study concluded that "opioid maintenance therapy can be a safe, salutary and more humane alternative to the options of surgery or no treatment in those patients with intractable non-malignant pain and no history of drug abuse."[3] High quality evidence demonstrating that opioids can be used safely for chronic non-terminal pain did not exist at that time. These reports eroded the historical evidence (see Appendix 2) of iatrogenic addiction and aversion to opioids, with the poor-quality evidence that was unfortunately accepted by federal agencies and other oversight organizations.

- **Pain patient advocacy:** Advocacy for pain management and/or the use of opioids[4,5,6] by pain patients was promoted, not only by patients, but also by some physicians. One notable physician stated: "make pain 'visible'… ensure patients a place in the communications loop… assess patient satisfaction; and work with narcotics control authorities to encourage therapeutic opiate use… therapeutic use of opiate analgesics rarely results in addiction."[7]

- **The opioid pharmaceutical manufacturing and supply chain industry:** One pharmaceutical company sponsored over 20,000 educational events for physicians and others on managing pain with opioids, claiming their potential for addiction was low.[8] Yet, warning signs of the addictive potential of oxycodone and similar opioids long predated this period: in 1963, Bloomquist wrote that dihydrohydroxycodeinone (oxycodone, Percodan®), "although a useful analgesic retains addiction potential comparable to that of morphine. This fact should be considered when it is prescribed. Because of increasing numbers of addicts to this drug in the State of California, the California Medical Association Committee on Dangerous Drugs and the House of Delegates has recommended that oxycodone-containing drugs be returned to the triplicate prescription list as they were originally in 1949." This recommendation failed to pass the legislature.[9] Similar warnings followed.

  Aggressive promotion of an oxycodone brand from 1997-2002 led to a 10-fold rise in prescriptions to treat moderate to severe noncancer pain, and increases in prescribing of other opioids. Subsequently, the highest strengths permissible was increased for opioid-tolerant patients, likely contributing to its misuse. Extended-release (ER) formulations and delayed absorption were marketed as reducing abuse liability, but crushing the pills allowed users to snort or inject the drugs.[10,11] There are now at least five marketed opioids that carry abuse-deterrent labeling. It has been hypothesized that the marked rise in heroin and other illicit synthetic opioids is, in part, associated with unintended consequences of reformulation of OxyContin, and a reduced supply and greater expense of prescription opioids.[12,13]

  To this day, the opioid pharmaceutical industry influences the nation's response to the crisis.[14] For example, during the comment phase of the guideline developed by the Centers for Disease Control and Prevention (CDC) for pain management, opposition to the guideline was more

common among organizations with funding from opioid manufacturers than those without funding from the life sciences industry.[15]

- **Rogue pharmacies and unethical physician prescribing:** The key contributors of the large number of diverted opioids were unrestrained distributors, rogue pharmacies, unethical physicians, and patients whose opioid medications were diverted, or other patients who sold and profited from legitimately prescribed opioids.[16]

- **Pain as the 'fifth vital sign':** The phrase, "pain as the 'fifth vital sign,'" was initially promoted by the American Pain Society in 1995, to elevate awareness of pain treatment among healthcare professionals; "Vital Signs are taken seriously. If pain were assessed with the same zeal as other vital signs are, it would have a much better chance of being treated properly. We need to train doctors and nurses to treat pain as a vital sign. Quality care means that pain is measured and treated."[17]

  The Veteran's Administration (VA)[18] and then the Joint Commission on Accreditation of Healthcare Organizations (the Joint Commission) designated pain as a 'fifth vital sign.'[19,20] The Joint Commission accredits and certifies health care organizations. Certification has implications for objective assessment of clinical excellence, and for contracting and reimbursement. The Joint Commission's standards for pain assessment in 2000 "were a bold attempt to address widespread underassessment and undertreatment of pain,"[21] even though the health care community was not advocating for a regulatory approach to pain management.[22] The standards raised concerns that requiring all patients to be screened for the presence of pain and raising pain treatment to patients' rights issue could lead to overreliance on opioids.

  The Joint Commission received sponsorship for developing educational materials from an opioid pharmaceutical company.[23] The pharmaceutical company funded over 20,000 pain-related educational programs either through direct sponsorship or financial grants. The Joint Commission was "unaware that the science behind their claims and the advice of experts in the field were erroneous."[24] This designation set in motion a growing compulsion to detect and treat pain, especially to prescribe opioids beyond traditional boundaries of treating acute, postoperative, procedural pain and end-of-life care. The surge in opioid supply escalated into opioid-related misuse, diversion, use disorder, and overdose deaths. Administrators, regulatory bodies, and insurers collectively pressured physicians to address patient satisfaction with aggressive pain management.[25] However, the concept that iatrogenic addiction was rare and that long-acting opioids were less addictive had been widely repeated, and studies refuting these claims were not published until years later. The Joint Commission has since eliminated the requirement that pain be assessed in all patients, except for patients receiving behavioral health care and established much stricter processes to review any corporate sponsorship of educational programs. In 2016, the Joint Commission began to revise its pain standards,[26] which will go into effect in January 2018.

- **Inadequate oversight by the Food and Drug Administration (FDA):** The FDA is the sole federal authority responsible for protecting public health by assuring the safety, efficacy, and security of human drugs, biological products, and medical devices. It approves medications to diagnose, treat, and mitigate illnesses, after assessing their safety and efficacy. It safeguards the nation's medications by setting standards for proper prescribing of approved drugs and post-approval surveillance. The FDA provided inadequate regulatory oversight. Even when overdose deaths mounted and when evidence for safe use in chronic care was substantially

lacking, prior to 2001, the FDA accepted claims that newly formulated opioids were not addictive, did not impose clinical trials of sufficient duration to detect addiction, or rigorous post-approval surveillance of adverse events, such as addiction.

The FDA also failed to assess the risks associated with deliberate diversion and misuse of opioids, risks that conceivably outweighed the intended benefits for patients if used as directed. They accepted the pharmaceutical industry's claim that iatrogenic addiction was "very rare" and that the delayed absorption of OxyContin reduced the abuse liability of the drug.[27] By 2001, the FDA removed these unsubstantiated claims from OxyContin's labeling. In March 2016, the FDA requested from the National Academies of Sciences, Engineering, and Medicine (NASEM) and received on July 13, 2017, a summary of the current status of science regarding prescription opioid abuse and misuse, and the role of opioids in pain management.[28] The current FDA Commissioner has stated a strong commitment to using the regulatory authority of the FDA to mitigate the adverse consequences of opioid use.[29]

- **Reimbursement for prescription opioids by health care insurers:** Sales of prescription opioids in the U.S. nearly quadrupled from 1999 to 2014,[30] largely paid for by insurance carriers. It is estimated that 1 out of 5 patients with non-cancer pain or pain-related diagnoses are prescribed opioids in office-based settings.[31] From 2007 to 2012, the rate of opioid prescribing steadily increased amongst specialists more likely to manage acute and chronic pain (pain medicine [49%], surgery [37%], physical medicine/rehabilitation [36%]). Insurance carriers, including Medicare Part D plans, did not serve as a stop-gap to the huge influx of opioid prescriptions.

- **Medical education:** Medical education has been deficient in pain management, opioid prescribing, screening for, and treating addictions.[32] During the 1990's, the pain movement should have alerted medical education institutions and creators of continuing medical education courses to address this issue. In some medical schools and some specialties, it remains inadequate to this day.[33] One strategy promoted 10 years ago to stratify patients' risk for opioid misuse and overdose was the screening of patients for substance use disorders (SUDs), especially pain patients.[34] Implementation of Screening, Brief Interventions, and Referral to Treatment (SBIRT) in healthcare systems was incentivized with billing codes.[35] SBIRT was mainstreamed into health care reform, but has yet to be incorporated nationally into medical curricula, or applied as routine care. Nor do core curricula necessarily address addictions, treatment options, or stress the need to screen for substance use and mental health.

- **Lack of patient education:** Patients and their families are not often fully informed regarding whether their prescriptions are opioids, the risks of opioid addiction or overdose, control and diversion, dose escalation, or use with alcohol or benzodiazepines.

- **Public demand evolves into reimbursement and physician quality ratings pegged to patient satisfaction scores:** Today, the use of opioids for chronic non-cancer pain remains controversial for the same reasons their use declined and was avoided at the turn of the 20th century: the potential for misuse and addiction, insufficient high-quality evidence of efficacy with long-term use, poor functional outcomes, overdose and death.

  Yet, a strong public demand for opioids continues to pressure clinicians to prescribe opioids persists. As an example, a recent survey of Emergency Department (ED) physicians indicated that 71% reported a perceived pressure to prescribe opioid analgesics to avoid administrative and regulatory criticism. Uniformly, they voiced concern about excessive emphasis on patient

satisfaction scores by reimbursement entities as a means of evaluating their patient management. The physician requirement to address pain as the "fifth vital sign" persists,[36] and reimbursement metrics based on patient satisfaction may have inadvertently created an environment conducive to exploitation by prescription opioid abusers.[37] There are legitimate circumstances for which opioids are an appropriate therapy. But many current institutional and societal issues continue to pressure physicians to prescribe opioids when they are not clinically appropriate.

Prior to this year, poor patient satisfaction with pain care could lead to reduced hospital reimbursement by Medicare through Value-Based Purchasing (VBP). There are often higher costs or no specific reimbursements for alternative pain management strategies, alternative pain intervention strategies, or spending time to educate patients about the risks of opioids. Further, failing to provide adequate pain relief can be grounds for malpractice claims or medical board action.

- **Lack of foresight of unintended consequences:** As prescription drugs came under tighter scrutiny and access became more limited (via abuse-deterrent formulations and more cautious prescribing), market forces responded by providing less expensive and more accessible *illicit* opioids. Increases in overdose death numbers due to prescription opioids have transitioned to overdoses largely due to heroin and, increasingly, fentanyl.[38] Locally, this trend may have been driven, in part, by tightening controls on prescription opioids. Physicians curtailed opioid prescriptions without guidelines on tapering and without determination of whether patients had developed an opioid use disorder (OUD), and if so, how to respond.[39]

  The availability of cheaper heroin also drove prescription opioid misusers to illicit opioids. Black market heroin is currently much less expensive than diverted prescription opioids, and fentanyl is even much less expensive per dose than heroin. Predictable from the economics of the two drug categories, the prescription drug overdose problem has decreased, but not the overall number of opioid-related deaths.

- **Treatment services insufficient to meet demand and to provide medication-assisted treatment (MAT):** As OUDs increased dramatically over the past 15 years, quality treatment services and the associated workforce did not expand in response to the growing crisis.

- **Lack of national prevention strategies:** Prevention strategies focusing on specific illicit drugs for vulnerable populations - adolescents, college age youth, pregnant women, unemployed men, and other - and for influencers, (parents, families) don't exist or have not been tested adequately.

Magnitude and Demographics

National statistics on prescription opioid misuse and use disorder, 2016.[40] Weighted *National Survey on Drug Use and Health* (NSDUH) estimates suggested that, in 2016, 91.8 million (34.1%) or more than one-third of U.S. civilian, noninstitutionalized adults used prescription opioids; 11.5 million (4.3%) misused them. In 2015, 1.6 million (0.7%) had an OUD. Among adults with prescription opioid use, 12.2% reported misuse and 15.1% of misusers reported a prescription OUD.[41] The most commonly reported motivation for misuse was to relieve physical pain (63.6%).

Misuse and use disorders were most commonly reported in adults who were uninsured, were unemployed, had low income, or had behavioral health problems. Among adults with misuse, 62.2% reported using opioids without a prescription, and 40.6% obtained prescription opioids for free from friends or relatives for their most recent episode of misuse. The results suggest a need to improve access to evidence-based pain management and to decrease excessive prescribing that may leave unused opioids available for potential misuse.[42]

The NSDUH estimates that 3.4 million people aged 12 or older in 2016 were *current* misusers of pain relievers (1.2% of the population aged 12 or older).[43] In 2016, an estimated 239,000 adolescents aged 12 to 17 were *current* misusers of pain relievers (1.0% of adolescents) and 631,000 young adults aged 18 to 25 misused pain relievers in the past month (1.8% of young adults). Among adults aged 26 or older, 2.5 million are estimated to be current misusers of pain reliever (1.2%). Upwards of 1.8 million Americans harbor an OUD involving prescription opioids or 0.7% of people aged 12 or older. Among adolescents aged 12 to 17, 152,000 (0.6%) had a pain reliever use disorder in the past year, and 291,000 young adults aged 18 to 25 (0.8%) and 1.3 million adults aged 26 or older in 2016 (0.6%) had a pain reliever use disorder in the past year. These small percentages do not convey the massive personal and public health burden created by misuse of opioids.

National statistics on heroin use and use disorder, 2016.[44] The addictive and illegal opioid heroin has no accepted medical use in the United States. Past 30 day users of heroin (475,000) among people aged 12 or older or 0.2% of the population is probably an underestimate because NSDUH surveys households and does not capture heroin users in homeless shelters or transient populations with no fixed address, and the incarcerated. Despite its dangers heroin use continues to escalate and reflects changes in heroin use by adults aged 26 or older and, to a lesser extent, among young adults aged 18 to 25. Less than 0.1% of adolescents aged 12 to 17 were current or past year heroin users (3,000 and 13,000, respectively) and these numbers remained relatively stable. Among young adults aged 18 to 25, 0.3% were current heroin users (88,000) and this number rose since 2002. For past year and at minimum, 630,000 individuals have a heroin use disorder (HUD).[17] Among adults 26 and older 0.2% were current heroin users (383,000), a rise since 2015. About 626,000 people aged 12 or older reported an HUD (0.2%), an increase since 2002 to 2011. Less than 0.1% of adolescents aged 12 to 17 (1,000) had an HUD in the past year, but this rate was many times higher among 18-25-year-olds (152,000; 0.4%). Approximately 473,000 adults aged 26 or older had an HUD (0.2%)

Substance use disorder treatment needs, 2016.[45] For NSDUH, people are defined as needing substance use treatment if they had an SUD in the past year or if they received substance use treatment at a specialty facility in the past year. In 2016, 10.6% of people aged 12 or older (2.3 million people) who needed substance use treatment received treatment at a specialty facility in the past year. Among people in specific age groups needing substance use treatment, 8.2% of adolescents aged 12 to 17, 7.2% of young adults aged 18 to 25, and 12.1% of adults aged 26 or older received substance use treatment at a specialty facility in the past year. These percentages represent 89,000 adolescents, 383,000 young adults, and 1.8 million adults aged 26 or older who needed substance use treatment and received treatment at a specialty facility in the past year. Prior to 2016, NSDUH reported on the reasons people in need in treatment did not receive it. Approximately 90% self-reported they did not feel the need for treatment and did not seek it.

Special Populations. The Commission recognizes that, although many of the recommendations included in this report are generic for the population as a whole, subpopulations exist within our

nation that conceivably require increased outreach, access to services, and more tailored or intensive services. These special populations can be viewed from the perspective of race or ethnicity, residential location and population density, gender, age[46], mental[47] and physical health status (e.g. HIV-AIDS), income, employment, socio-economic status, education, veterans,[48,49] involvement in the criminal justice system (juveniles, parolees, incarcerated), family status (fetus[50], children of substance-using parents or other family members, pregnant women, living alone), healthcare insurance sources, behavioral health indicators[51] (other SUDs or history), type of opioid use (heroin/fentanyl, prescription opioid nonmedical or medical use, or combined use), and others.

According to the 2016 NSDUH, more males (4.8%) than females (3.8%) misused prescription opioid medications.[52] Young adults aged 18 to 25 years old had the largest proportion of misusers. In comparison to the national average for past year misuse of pain relievers by those 12 years and older, misuse was most common among Americans with two or more races (6.5%), American Indian or Alaska Natives (3.9%), Native Hawaiian or other Pacific Islanders (4.2%), and Hispanics (4.2%). The rate of non-medical use of prescription opioid medications was lowest among Asians (1.8%).

Scrutiny of the NSDUH and other data sources can reveal which populations are at highest risk. A recent study using 2010-2013 NSDUH data[53] revealed the prevalence of OUDs was highest among whites (72.29%), with lower prevalence among blacks (9.23%), Hispanics 13.82%, and others 4.66%. Other factors overrepresented among those reporting OUDs were adults aged 18–34 (55.95%), males (57.39%), low income (<$50,000; 67.12%), residents of large metropolitan areas (49.99%), with fewer privately insured persons (40.97%). Compared with whites, adolescents were overrepresented among mixed-race persons and Hispanics. In contrast, Native Americans included a higher proportion of older adults aged≥50.[54] Among mixed-race persons, the proportion of females was higher than males. The vast majority of blacks (83.78%), Native Americans (88.98%), and Hispanics (76.44%) were in the lowest income group. A high proportion of blacks, Native Hawaiians/Pacific Islanders/Asian Americans, and Hispanics resided in large metropolitan areas. A high proportion of native-Americans lived in nonmetropolitan areas. All non-white groups, except for Native Hawaiians/Pacific Islanders/Asian Americans, had higher proportions of public insurance than whites.

Among persons with OUD, the majority (80.09%) had another SUD, 28.74% had major depression, 53.02% had nicotine dependence, 40.93% had alcohol use disorder (AUD), and 43.22% had ≥1 other drug use disorder (cannabis 22.32%, tranquilizer 13.99%, cocaine 15.25%, stimulant 9.28%, hallucinogen 5.25%, sedative 3.51%, inhalant 2.22%), which was more prevalent among whites (83.39%) than Hispanics (72.04%). Major depressive episode was also common (28.74%). Most people with OUD report no use of OUD treatment, with only 26.19% using any alcohol or drug use treatment, 19.44% using opioid-specific treatment. Adolescents, the uninsured, blacks, Native Hawaiians/Pacific Islanders/Asian Americans, persons with prescription opioids only, and persons without depression episodes especially underutilized opioid-specific treatment. The treatment rate for adolescents among blacks with OUD was very low, unless they were involved with the criminal justice system. Among alcohol/drug use treatment users, self-help group and outpatient rehabilitation treatment were commonly used services.

Adolescent-onset OUD indicates a high risk for severe OUD. Low treatment rates, conceivably related to inadequate MAT data for adolescents, places this population at particular susceptibility. Native Hawaiians/Pacific Islanders/Asian Americans with OUD had the lowest prevalence of

using alcohol/drug treatment (4.91%) or opioid-specific treatment (1.24%). Cultural-related stigma toward addiction and a lack of culturally congruent addiction providers are unique barriers to seeking treatment. Residents in rural areas have relatively high rates of opioid overdoses, but they face substantial barriers to OUD treatment, including a shortage of mental/behavioral health providers.

Newly Emerging Threats

New Psychoactive Substances. The term "new psychoactive substances" (NPS) can be defined as individual drugs in pure form or in complex preparations that are not scheduled under the *Single Convention on Narcotic Drugs* (1961) or the *Convention on Psychotropic Substances* (1971). NPS may be categorized by chemical structure, by psychoactive properties, by biological targets, or by source (plant, synthetic, or combined). The emergence of NPS that target opioid sites in the body is challenging public health and drug policies globally. Their novelty, ambiguous legal status, ability to evade toxicological tests, swift adaptation to legal restrictions, global internet marketing, and scant public knowledge of their adverse effects are among the key drivers of this 21st century phenomenon.

The designation "new" is not necessarily limited to newly-designed compounds with no historical precedent, but may also include compounds modified from substances previously used. The majority are chemical analogs of drugs in restricted categories and may elicit effects similar to the parent drug, or a more amplified response. Others may evoke unique or complex sensations because of their hybrid structures, or because several compounds with differing pharmacological profiles are combined and sold as a unit. Although synthetic cathinone analogs and synthetic cannabinoids occupy a major share of this market, synthetic opioids, especially fentanyl analogs, are by far the most problematic substances because they are emerging as a leading cause of opioid overdose deaths in the United States.[55]

Drivers of NPS. The rapid expansion of NPS in the past decade is fueled by a convergence of the information revolution, vague legal status, uncertain detectability, and financial incentives combined with guileful marketing.[56]

The internet is a "global neural network" that can be exploited to disseminate promotion and distribution of these drugs instantly. The venues are chat rooms, blogs, instant messaging sites, social networking, or multimedia sites. At minimal cost, descriptions of new drugs, their positive psychoactive effects, doses, synthetic routes, and purchasing sites are accessible world-wide on computers or mobile devices such as smart phones or smart watches. Many of the marketing sites are impervious to legal sanctions, as it takes time to deliberate the evidence and move newly emerging drugs into a legally restrictive zone, especially internationally.

Imperfect international agreements and a gradual dissolution of international resolve to attenuate drug use compromise effective solutions to this unique problem. Often, substances that imitate controlled drugs are unscheduled, unregulated, and not under the auspices of international law. Their nebulous legal status is an incentive for entrepreneurs to introduce new drugs quickly into the global market.

The allure of NPS is magnified by current limitations in detecting them. Identifying these drugs for forensic, workplace, legal, and policy purposes is constrained by a lack of reference materials

and the need for sophisticated detection methods which are not routinely available (e.g., mass spectroscopy). The chemical structures of NPS are designed to keep one step ahead of federal and international laws that restrict distribution and sale of specific chemicals. The Drug Enforcement Administration (DEA) has emergency powers to temporarily schedule a drug for 36 months, a time frame to accumulate evidence for/against long-term drug scheduling.

New Psychoactive Opioids. Novel opioid receptor agonists, some of which are much more potent than morphine, are of particular public health concern, as they can be mixed with or substituted for heroin, and are more likely to be deadly.[57] As these novel opioids emerge, emergency responders, medical professionals, law enforcement personnel, death investigators, medical examiners, toxicologists, and prosecutors face the challenge of treating and investigating intoxications and deaths from novel compounds whose identities are often unknown and for which analytical standards do not exist.

In 2013, the rapid ascent of the potent opioid agonist fentanyl compelled a rethinking of public health and regulatory approaches to the opioid crisis.[58] Fentanyl and fentanyl analogs, including carfentanil, are becoming a major contributor to opioid overdose fatalities in specific states, especially in the eastern half of the nation.[59] Many have been identified, with some fentanyl analogs found as contaminants of other drugs, e.g. furanyl fentanyl has been identified as a contaminant in crack cocaine.[60,61,62,63,64] As many do not cross-react in routine assays, a simple analytic device to identify whether a street drug is unknowingly contaminated with fentanyl analogs may yield a false negative and a false sense of security.

Other opioid NPS compounds include U-47700 (‘pink’), U-50488, desomorphine, salvinorin A, and its analog herkinorin.[65] ‘Krokodil,’ the street name for a homemade cheap heroin substitute in Russia, is synthesized from codeine, iodine, and red phosphorus, with esomorphine claimed as the end product. A total of 54 morphinans were detected after detailed chemical analysis, highlighting the possibility that additional morphinans may contribute to the psychotropic effects of krokodil.[66]

Pathways to Opioid Use Disorder (Including Heroin) from Prescription Opioids

Prior History of Prescription Opioid Misusers Who Seek Treatment. In 2016, 91.8 million people (ages 12 or older) in the United States use pain relievers in the past year.[67] Of these, 11.5 million people reported misuse of pain relievers.

In an analysis of more than 4,400 patients entering drug treatment for opioid abuse, of individuals initially exposed to opioids through a physician's prescription to treat pain, 94.6% had used a psychoactive substance non-medically prior to or coincident with their opioid prescription. Alcohol (92.9%), nicotine and/or tobacco (89.5%), and marijuana (87.4%) were used by nearly all patients prior to, or coincident with, their first opioid prescription. If one excludes these drugs, 70.1% (n=2,913) still reported some psychoactive drug use of licit or illicit stimulants (77.8%), benzodiazepines (59.8%) or hallucinogens (55.2%).[68] Similar findings were observed in a study restricted to women.[69] The findings are consistent with concerns that persons with prior use of addictive substances are at considerably higher risk for prescription opioid misuse, with addiction to one substance alone uncommon.[70] It highlights the need for clinicians to screen patients for prior

drug use histories and judicious monitoring of and intervention with these at-risk patients prior to or during opioid prescribing. There is abundant evidence is that increased risk of iatrogenic addiction or nonmedical use of prescription drugs overlaps consistently with problematic drinking, marijuana use, and other forms of substance use or a history of substance use or use disorder.

Prescription Opioids and Transition to Prescription OUD. Understanding the risks factors that drive transition to an OUD are critical for developing effective policies to attenuate the process.[71,72] The specific opioid, the dose, number of doses, duration, route of administration, formulation, ER, or immediate-release (IR) can influence misuse and progression to addiction. Some opioids engender greater likability or abuse liability than others. In patients dependent on heroin, oxycodone was ranked highest of several opioids, while buprenorphine scored lowest.[73] Overall, the risk of transition from medical use for pain relief to dependence is especially high for opioids, especially with longer use, and high doses.

One study found that the probability of long-term prescription opioid use increased markedly in the initial period of therapy, especially after five days or one month.[74] One causative factor of addiction is the development of rapid tolerance which can progress to OUD, without careful tapering.

In a small study of a single population, patients self-reported five common pathways to OUD: (1) inadequately controlled pain; (2) initial exposure to opioids during acute pain, which triggered a unique positive response; (3) relief from emotional distress; (4) relapse to a prior opioid addiction triggered by prescription opioids; and (5) misuse of prescription opioids solely for psychoactive purposes.[75] This survey highlights the need for prescribing clinicians to screen patients for prior history of substance use.

Prescription Opioids and Heroin Use Disorder. The vast majority of patients who use prescription opioids, either short or long term, do not progress to misuse and are unlikely to transition to heroin use. If transition occurs, the reverse (heroin to prescription opioids) is rare, as heroin is less expensive, more euphoric by the intravenous route, and more accessible. Overprescribing is still considered a driver of increases in opioid-related consequences, addiction, overdose, and infections, as it sustains nonmedical use of prescription opioids.[76,77] However, heroin initiation occurs in a relatively small subgroup of nonmedical users of prescription opioids,[78,79,80] but nonmedical use is a key risk for conversion to heroin use.[81,82] Although the percent of annual conversions from the large number of prescription opioid users to new heroin users is low, approximately 80% of heroin users are estimated to have transitioned from misuse of prescription opioids in recent years.[83,84]

Transition to heroin use among young prescription opioid users was predicted by prescription OUD, use of prescription opioids at an early age, and recreational use for psychoactive purposes. More specifically, a nationally representative sample of U.S. adolescents (2004-2011 NSDUH; n = 223,534; aged 12-21 years), showed that a prior history of nonmedical use of prescription opioids was strongly associated with heroin initiation, with the highest risk being nonmedical use of prescription opioids at ages 10-12 years, regardless of race/ethnicity or income group.[85] Moreover, because the peak period of heroin initiation occurs later, efforts to prevent heroin use may be most effective if they focus on young people who already initiated nonmedical use of prescription opioids.

An association between policies related to curtailing prescription opioids and heroin use or overdose mortality has yet to be definitively shown. Research has not yet shown whether

restrictions on prescribing increased heroin use among those who had already initiated heroin. Yet, past year heroin use among nonmedical opioid users has increased dramatically among young adults and emerging adults during the past six years.[86]

In one study of people in treatment, more persons (33.3%) in 2015 were experimenting with heroin as their first opioid exposure compared with 10 years prior (8.7%), although they may differ from the general population of opioid users.[87] In the same period, their endorsement of oxycodone and hydrocodone misuse declined. As supply side interventions reduce accessibility to commonly prescribed opioids, some initiates replace prescription opioids with heroin. Imprecise heroin dosing in users without a history of opioid use may contribute to overdose fatalities in novices. Fentanyl and analogues may be too strong for all but the most tolerant opioid users. Nearly half of patients entering treatment for OUD reported first exposure to opioids through a physician's prescription for pain management,[88] but these estimates may need revision in view of currently high availability of heroin and fentanyl.

Heroin Use. Heroin use also increased during the same period that witnessed a rise in prescription opioid misuse. Data from the 2001-2002 and 2012-2013 *National Epidemiologic Survey on Alcohol and Related Conditions-I and–III* (NESARC) showed prevalence of heroin use increased five-fold and use disorder tripled in the United States during the period between the two surveys.[89] The rise was greater among whites, unmarried respondents, males, young users, those with lower educational achievement, and those living in poverty. Prior exposure to nonmedical prescription opioids increased among white heroin users, reinforcing concerns and other reports that prescription opioid misusers were transitioning to heroin use. Evidence is accumulating that heroin is increasingly being used without prior to exposure to prescription opioids.[90]

Health, Financial, and Social Consequences

General Consequences of Opioid Misuse and Use Disorder. Heroin and other illicit opioids confer a high risk for medical consequences.[91] Nonmedical users of prescription pain relievers are 40 times more likely than the general population to use heroin or other injection drugs. Opioid addiction is a chronic difficult-to-treat disorder characterized by frequent relapses. Crude mortality rates and the risks of death of opioid users are substantially higher than the general population worldwide, although sample and country-level variables impact the extent and causes of mortality. Elevated causes of mortality among opioid users include overdose, traumatic and suicide deaths, and HIV-related mortality. Treatment, HIV-negative serostatus, and lower levels of injecting are protective factors against premature death.[92]

Powerful environmental factors can shape the course of heroin addiction. A study found that of the heroin-dependent soldiers who returned to the United States after the Vietnam War, only 12% were still drug dependent three years later.[93] Although more than half of the returning soldiers tried narcotics again, only a minority of them became re-addicted. These results illustrate that powerful environmental factors may influence the course of heroin addiction.[94]

Stable abstinence is less than 30% after 10-30 years, and even if abstinent, use of other drugs including alcohol is frequent.[95,96] Family, social support, and employment are associated with improved recovery rates, whereas a history of sexual or physical abuse and comorbid mental disorders correlate with persistent opioid use.[97,98,99]

A five-year abstinent period is associated with an increase in likelihood of stable abstinence. Mortality is 6-20 times higher than that of the general population, with deaths depending on country of origin. In the United States, the primary cause of mortality is overdose deaths.[100]

Medical Consequences. Opioid users are less healthy from the perspective of physical and mental health than drug users who do not use opioids.[101] They are also substantial users of medical services at higher costs than non-users and require chronic medical, psychiatric, and addiction care. Those using non-prescribed opioids differ from persons using opioids as prescribed, with more severe drug problems, as manifested by higher intravenous drug use and behavior that puts them at higher risk for HIV and Hepatitis C.

Opioid users have higher numbers of ED visits, more inpatient hospital stays, along with almost double the inpatient costs compared to their non-opioid using counterparts. Current data out of North Carolina indicates both a record number of overdose patients visiting EDs and that half, 49% of overdose survivors seen in the ED, do not have insurance.

Opioid users also have a higher mean number of outpatient medical visits and higher associated costs over the same time period. Their self-reported health status is lower, and they have a higher number of chronic medical comorbidities than their non-opioid using counterparts. They were also more likely to have been prescribed medication for psychological/emotional problems in their lifetime and to have a mental illness diagnosis.[102] Patients using opioids are more likely to be taking two or more illicit or non-prescribed drugs, to be taking non-prescribed benzodiazepines, and to report intravenous drug use. Compared to patients using opioids only as prescribed, those using any non-prescribed opioids were more likely to have been homeless, have more serious drug problems than those using opioids only as prescribed, engage in intravenous drug use, and have a higher HIV risk-taking score. Non-prescribed opioid users also had more problem alcohol use relative to their prescribed opioid user counterparts.

Infections and infectious diseases. Although overdose contributes most to drug-associated mortality, infections stemming from intravenous drug use are another major cause of death or an illness requiring hospitalization.[103,104,105] Injecting drug users are at risk for acquiring hepatitis C virus (HCV) and HIV, as well as invasive bacterial infections, including endocarditis.[106,107]

Brain Toxicity. Brain toxicity is a common finding for specific drugs of abuse.[108,109,110,111] Diagnostic imaging, especially magnetic resonance imaging (MRI) can detect a range of brain abnormalities associated with heroin use, including neurovascular complications related to inadequate blood supply such as stroke. A rare form of leukoencephalopathy has also been shown in people inhaling heroin vapors.

Children at risk. Children are at high risk in opioid-using environments. Pregnant women who continue to use opioids throughout the gestational period are likely to deliver a newborn with neonatal abstinence syndrome (NAS). The incidence of NAS is increasing in the United States, and carries an enormous burden in terms of hospital days and costs.[112] In comparing infants with a diagnosis of NAS with non-NAS infants between 2003 and 2012, NAS admissions increased more than fourfold, resulting in a surge in annual costs from $61 million and 67,869 hospital days in 2003 to nearly $316 million and 291,168 hospital days in 2012. For an infant affected by NAS, the hospital stay was nearly 3.5 times as long (16.57 hospital days compared with 4.98 for a non-NAS patient) and the costs more than three times greater ($16,893 compared to $5,610 for a non-affected infant).[113]

Children living in homes with drug abusers have numerous challenges, including the potential for exposure to drug production, chemicals, or equipment, neglect because the caregiver is using, abusive behavior towards the child,[114] risk of removal from their family, and/or exposure to the criminal sale or distribution of drugs.[115,116]

Labor Force. The Labor Force Participation Rate has declined since 2007, primarily due to an aging population and effects of the Great Recession. However, a recent Brookings Institution study examining the implications of the opioid crisis on the labor force suggests that the increase in opioid prescriptions could account for much of the decline in the labor force participation of "prime age men" (ages 25-54) during this same time.[117] The Bureau of Labor Statistics Time-Use Survey finds that 44% of prime age men not in the labor force acknowledged taking pain medications the previous day. The Brookings study found similar results (47% took pain medication the day before), however, nearly two-thirds of those men indicated it was *prescription* pain medication. Thus, on any given day, 31% of prime age men not in the labor force take prescription pain medication, most likely opioid based. These percentages are likely lower than the actual proportion of men who consume pain medication, due to the sigma and legal risk associated with narcotics.

Financial, Educational, Workplace, and Criminal Justice System. Prescription opioid overdose, abuse, and dependence carry high costs. In 2013, it was estimated that the total economic burden was $78.5 billion (in 2013 dollars).[118] Approximately one-third of the costs of the prescription opioid crisis are attributable to health care, and one-fourth of costs are borne by the public sector. Using data from various sources, the "monetized burden" of prescription opioid overdose, abuse, and dependence was estimated from a societal perspective, including direct healthcare costs, costs related to loss productivity, and costs to the criminal justice system. Total spending for health care and substance abuse was over $28 billion, most of which ($26 billion) was covered by insurance. In nonfatal cases, costs for lost productivity, including reduced productivity for incarcerated individuals, were estimated at about $20 billion. Fatal overdose costs related to healthcare and lost productivity were estimated at $21.5 billion. Approximately 25% of the economic burden was borne by public sector (Medicaid, Medicare, and veterans' programs) and other government sources for substance abuse treatment. Criminal justice-related costs were estimated at $7.7 billion expended by state and local governments in addition to lost tax revenue. The total estimated economic burden for prescription opioid abuse, addiction, and overdose death and heroin addiction would be approximately $111 billion (in 2013 dollars). Many costs are inestimable, including the social impact on opioid-dependent people, and the suffering of family members as witnesses to addiction or to fatal overdose.

Drug Overdose Deaths

The crisis in opioid overdose deaths has reached epidemic proportions in the United States (33,091 in 2015), and currently exceeds all other drug-related deaths or traffic fatalities. These data from the CDC are expected to rise even higher for 2016.[119] The risk of overdose resides primarily, but not exclusively, among those harboring a medical diagnosis of an OUD.[120] Of six risk markers (sex, age, race, psychiatric disorders, SUDs, urban/rural residence), SUDs have the strongest association with drug overdose death, followed by psychiatric disorders, white race, 35-44 year age group, and male sex.[121] Opioid-related death rates are higher among those who had recently been released from prison, those who doctor-shop and receive opioid prescriptions from multiple

pharmacies, and those who consume prescription opioids in combination with other scheduled medications, particularly benzodiazepines. From 1999 onwards, overdose deaths due to prescription opioids rose incrementally and consistently outpaced annual heroin death rates.

Heroin overdose deaths remained relatively low from 1999 onwards, and then escalated 4-fold from 2010-2015. Data from death certificates in 2015 revealed a disproportionate rise from the previous year in deaths attributable to fentanyl/analogs (72.2%) and heroin (20.6%), with prescription opioid-related deaths rising minimally (2.6%).

The overall death rate was higher for prescription opioids, but the most recent data show minimal increases in deaths involving prescription overdoses, while an increasing proportion now involves synthetic opioids, mainly fentanyl. Clearly, contamination of the heroin supply with fentanyl is currently driving recent increases in opioid-related overdose deaths. Reports from individual states in 2016 and 2017 confirm this emerging trend, as heroin and/or fentanyl currently account for more than 50% of the overdose deaths in specific states.[122]

Substance Use Treatment Availability

Among the many consequences of opioid misuse is the increasing need for SUD treatment services. SUD treatment facilities, particularly those providing MAT-enhanced opioid treatment programs (OTP), are uncommon in rural areas, as are physicians who can provide MAT from their offices.

Across all U.S. counties, 38% did not have a treatment facility for SUD in 2016 (Table 1).[123] Ten percent of large central metro counties did not have an SUD treatment facility. The data show that progressively larger proportions of counties did not have SUD treatment facilities as the level of urbanization decreased. Among the most rural counties, 55% did not have a substance use treatment facility. Figure 1 below shows counties that did not have an SUD treatment facility as of 2014 by level of urbanization, and it is clear that the vast majority of counties is rural.

Table 1. Treatment Facilities for Substance Use Disorder by Level of Urbanization, 2016

Level of Urbanization	*Number of Counties*				*Percent of Counties in Level of Urbanization*			
	Total	*No Treatment Facilities for Substance Use Disorder (SUD)*	*No SUD Treatment Facilities with Opioid Treatment Programs*	*No SUD Treatment Facilities that accept Medicaid*	*Total*	*No Treatment Facilities for SUD*	*No SUD Treatment Facilities with Opioid Treatment Programs*	*No SUD Treatment Facilities that accept Medicaid*
Large Central Metro	68	7	8	7	100%	10%	12%	10%
Large Fringe Metro	368	88	259	104	100%	24%	70%	28%
Medium Metro	373	100	242	116	100%	27%	65%	31%
Small Metro	358	100	267	121	100%	28%	75%	34%
Micropolitan (non-metro)	641	157	586	204	100%	24%	91%	32%
Non-core (non-metro)	1,333	728	1,321	800	100%	55%	99%	60%
United States	*3,141*	*1,180*	*2,683*	*1,352*	100%	38%	85%	43%

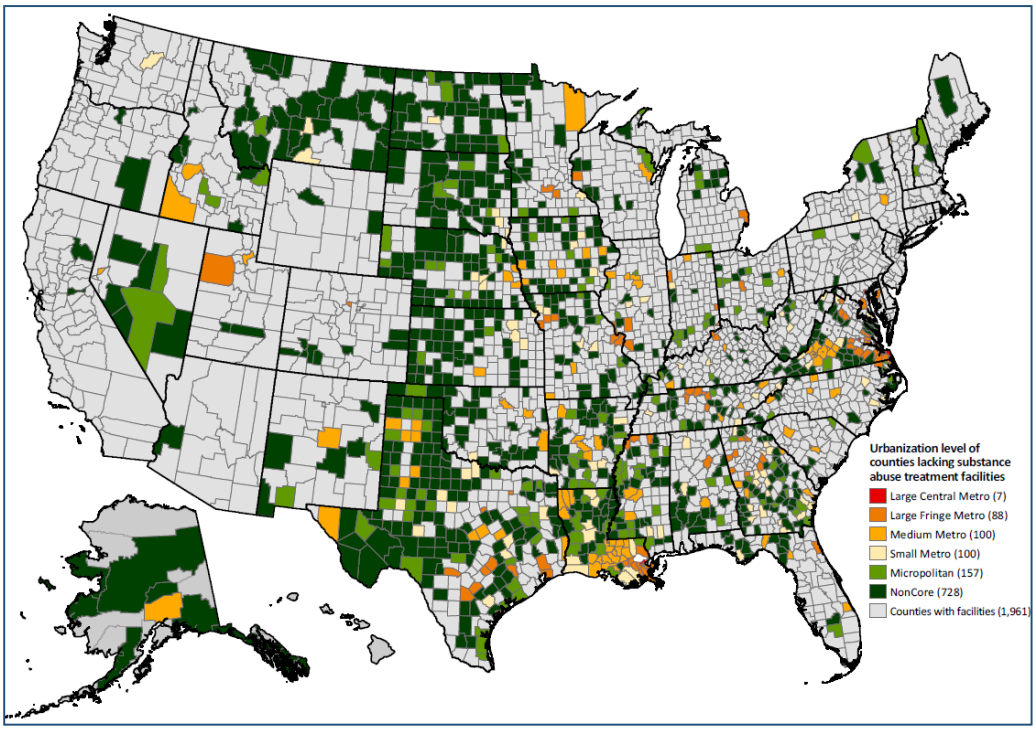

Figure 1. Counties with No Treatment Facilities for Substance Use Disorder by Level of Urbanization

Furthermore, 85% of all U.S. counties have no OTPs that provide MAT for people diagnosed with an OUD (Table 1). These facilities are concentrated in large central metropolitan areas, where 88% of these counties have at least one treatment facility offering OTP (only 12% of these central metropolitan counties do not have OTP facilities). For other metropolitan counties, 65 to 75% do not have OTP facilities, but among rural counties, almost all (91 to 99%) lack an OTP facility.

Figure 2 shows counties that did not have an OTP facility as of January 2016; as with SUD treatment facilities generally, the vast majority of these are rural counties. Many large fringe and medium metropolitan counties appear as doughnut-shaped areas around core locations where OTP facilities are located, but many rural counties are located far from OTP facilities.

Data were also obtained on the locations of physicians that can dispense buprenorphine from their offices.[124] Physicians can provide MAT for OUD treatment in settings other than OTP facilities, including dispensing buprenorphine from their offices. To prescribe or dispense buprenorphine for OUD treatment, qualified physicians must receive waivers from the DEA under the terms of the *Drug Addiction Treatment Act of 2000* (DATA 2000). As of February 2016, 47% of counties nationwide did not have a waived physician (Table 2). However, when classifying the county locations of waived physicians according to level of urbanization, the rural-urban disparities become clear. None of the large central metro counties, and 72% of the most rural counties, did not have a waived physician (Figure 3). The vast majority of counties without buprenorphine-waived doctors are rural. However, it is worth noting that the number of patients a physician can treat with buprenorphine is capped; so, having a waived physician within a geographic area is not necessarily indicative of sufficient access for county or city residents.

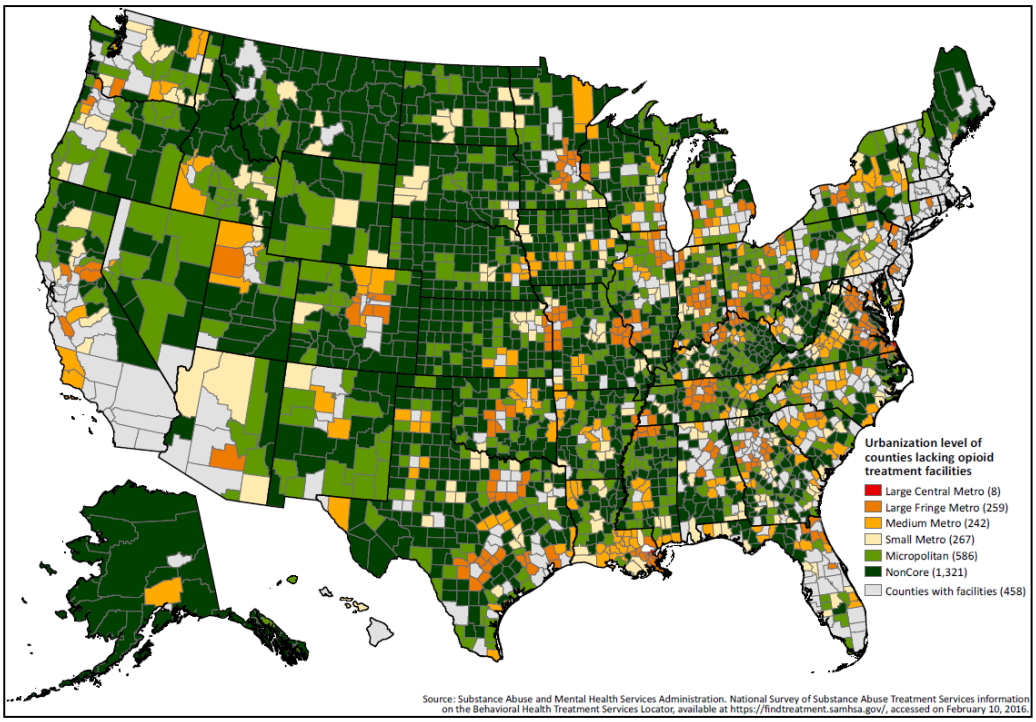

Figure 2. Counties with No Opioid Treatment Program Facilities by Level of Urbanization

While utilization of SUD treatment services in both rural and urban areas is challenged by many factors, the nature of these challenges varies. For example, findings from focus groups of counselors in rural areas noted a dearth of good facilities, poor access due to clients living far away from treatment centers, reliance on friends or family for transportation, and a need for basic medical and dental services. These factors were not mentioned by urban counselors.[125] A recent study of SUD treatment facilities that accept Medicaid also found that rural residents are less likely to have such a facility.[126]

Table 2. Physicians Waived to Dispense Buprenorphine by Level of Urbanization, 2016

Level of Urbanization	*Number of Counties*				*Percent of Counties in Level of Urbanization*			
	Total	*No Waived Doctors*	*1-5 Waived Doctors*	*More than 5 Waived Doctors*	*Total*	*No Waived Doctors*	*1-5 Waived Doctors*	*More than 5 Waived Doctors*
Large Central Metro	68	0	0	68	100%	0%	0%	100%
Large Fringe Metro	368	86	107	175	100%	23%	29%	48%
Medium Metro	373	107	86	180	100%	29%	23%	48%
Small Metro	358	113	103	142	100%	32%	29%	40%
Micropolitan (non-metro)	641	219	332	90	100%	34%	52%	14%
Non-core (non-metro)	1,333	964	340	29	100%	72%	26%	2%
United States	*3,141*	*1,489*	*968*	*684*	100%	47%	31%	22%

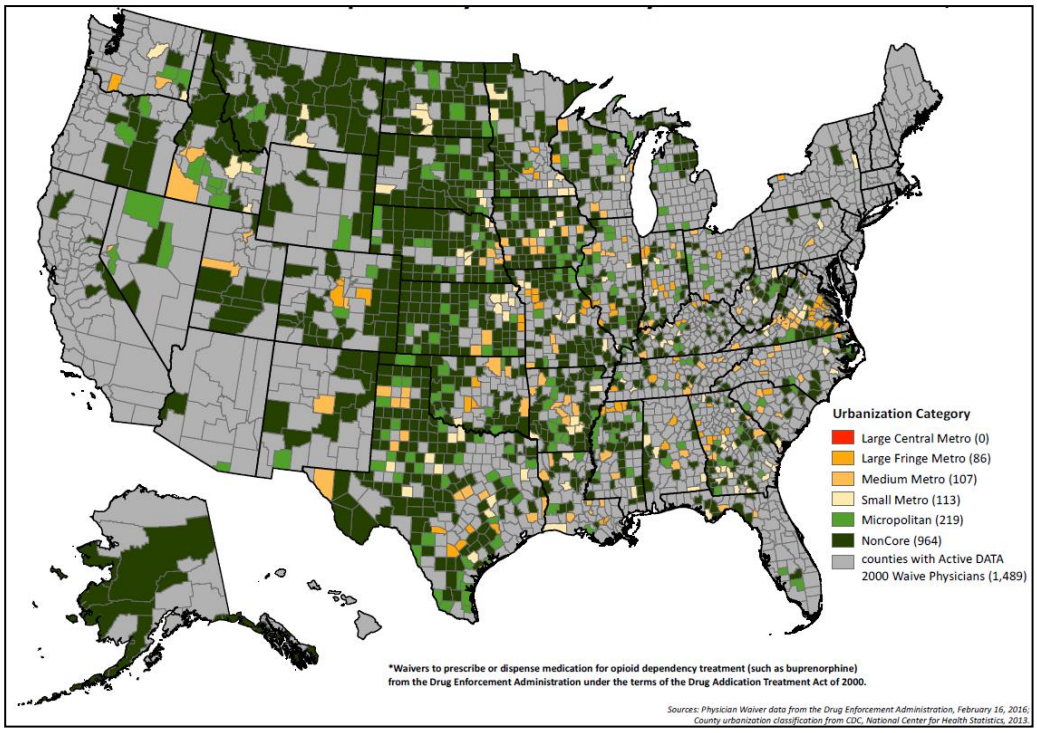

Figure 3. Counties with No Physicians with Buprenorphine Waivers by Level of Urbanization, 2016

Systems Approach to Solutions

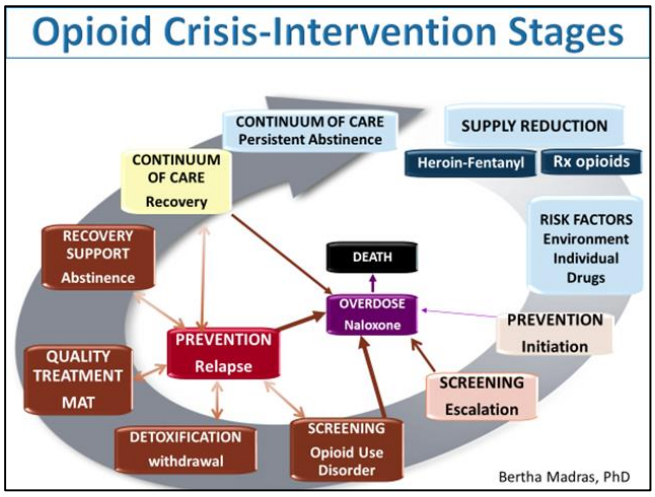

Figure 4. Opioid Crisis-Intervention Stages

There has never been a time more appropriate or opportune to develop effective and cost-effective policies for addressing substance use and disorders in our nation. A systems approach can facilitate development of recommendations and solutions to this dynamic and ever-shifting challenge. This report addresses solutions to each of the core components of the crisis, a trajectory which begins with drug supply, attitudes towards drug use and knowledge of opioids, risk factors for misusing, and progresses to addiction, transition to heroin/fentanyl, situational factors in overdose, rescue, treatment, relapse prevention, recovery support, and continuum of care (Figure 4). Over the past decade, large databases have accumulated to inform policies and associated budgets.

The most urgent goals and readily quantifiable achievements will be a reduction in overdose episodes and deaths, increased entry into and adherence to high quality treatment, and a reduction

in prescribed opioids. More complex models are needed to address whether prescribing policies result in time-dependent reductions in prescription opioid diversion or increase heroin/fentanyl use, who is at risk for transitioning to heroin or fentanyl, the incidence and prevalence of OUD, and others. The opioid epidemic defies standard medical and legal models for addressing addiction and trafficking. Limited data exists to track the crisis and identify weaknesses in current responses (e.g. prescribing practices, treatment availability, individuals at risk), but is held in different databases across a multitude of public and private organizations, and significant proportion is not in real-time.

Building a secure data foundation that promotes cross-entity collaboration while protecting privacy is a challenging but necessary step to save lives, expand treatment options, and effectively prevent further spread of this deadly epidemic. The data exists but resides in agency silos, or in the private sector providing analytics for specific industries (e.g. pharmaceutical or healthcare insurers), making it difficult to act upon the information. **The Federal Government should create an integrated data environment that brings together publicly available data with agency-specific data to help address this epidemic.** Often, the same data viewed through a different lens can support multiple parts of the problem. For example, doctors can use prescription drug monitoring programs (PDMPs) to check patient records, while law enforcement can use PDMPs to identify prolific opioid prescribers and public health agencies can use it to identify and intervene in a potential victim pool before overdoses occur – different, but all valuable uses of the same data.

This kind of effort would not require a new data warehouse or standardization initiative; the integrated data environment can immediately integrate existing data sources.

Federal Funding and Programs

On page 93 of the report, there is a full breakdown of federal funding sources for drug-related activities, including interdiction, prevention, and treatment. As shown in that section, the federal funding landscape is complex, exists in silos, potentially duplicative, and supports hundreds of on the ground programs.

Streamlining Federal Funding for Opioids and Consideration of State Administrators

One of the first activities the Commission Chair undertook was a series of calls with Governors' Offices in nearly all 50 states. A number of themes emerged from those calls that are reflected in this report and the recommendations. Regarding funding, many Governors and senior staff members expressed concern at how addiction and opioid-related funding coming from the Federal Government was fragmented; provided by many different agencies and funding sources which each had their own application requirements, reporting mechanisms, and preferred outcomes.

It is clear that each federal agency has goals related to reducing drug use and misuse and provides funding for such activities. However, from the vantage points of states, this funding is not well coordinated, and applying for funding from the many different agencies, is a tremendous administrative burden for states.

The SAMHSA block grants provide a formula-based grant to states for treatment activities; if additional funding opportunities could be rolled into the SAMHSA block grant, or combined to form larger block grants that required one application and one set of reporting requirements, that would free up state resources to focus on implementation activities, rather than paperwork.

Some states have identified a State Administrator to coordinate opioid and addiction activities. Others may use their Single State Authorities for substance abuse services to serve as an effective point of contact or liaison regarding most federally-supported demand reduction efforts in a state—although they may not always have up-to-date information on Department of Health and Human Services (HHS) or Department of Justice (DOJ) discretionary grant activities not directly involving the state. Regardless of the single entity that is identified by the state, the Federal Government should have a comparable single entity point of contact to help track activities related to discretionary grants with a demand reduction focus.

The Office of National Drug Control Policy's (ONDCP) core function is to develop and coordinate the implementation of national drug policy, but it does not have appropriate staff or organizational units to track federally supported demand reduction funding and activities at the program or grant level (versus the overarching policy level). The tasks of making and tracking grant awards fall squarely within the responsibility of the Departments and agencies that manage grant programs, including HHS's Regional Offices and the more recently established Substance Abuse and Mental Health Services Administration (SAMHSA) Regional Directors stationed in these offices. It therefore would seem reasonable for HHS to support ONDCP in this function by serving as an intermediary with Single State Authorities in the 50 states, the District of Columbia, and the territories. By so leveraging HHS and SAMHSA regional infrastructure, ONDCP could maintain timely accounting and ongoing awareness of the current allocation of federal demand reduction funding and the coordination of federally supported initiations, their contribution to activities

funded at the state and local level, duplication or inefficiencies that may need to be addressed, and timely scrutiny the program effectiveness of federally-or-state-funded programs. This would assist ONDCP to become aware of promising practices emerging at the state level.

1. **The Commission urges Congress and the Administration to block grant federal funding for opioid-related and SUD-related activities to the states, where the battle is happening every day. There are multiple federal agencies and multiple grants within those agencies that cause states a significant administrative burden from an application and reporting perspective. Creating uniform block grants would allow more resources to be spent on administering life-saving programs. This was a request to the Commission by nearly every Governor, regardless of party, across the country.**
2. **The Commission believes that ONDCP must establish a coordinated system for tracking all federally-funded initiatives, through support from HHS and DOJ. If we are to invest in combating this epidemic, we must invest in only those programs that achieve quantifiable goals and metrics. We are operating blindly today; ONDCP must establish a system of tracking and accountability.**

Funding Effective Opioid-Related Programs

As stewards of taxpayer dollars, the Federal Government must ensure that programs demonstrate effectiveness in achieving the desired policy outcomes. While various assessments have demonstrated that treating and preventing substance use are effective in reducing the costs associated with health care, the workplace, and criminal justice system, these costs-benefit analyses were done at the system, not program, level.

At the program level, the Federal Government has a long history of undertaking a variety of efforts, varyingly referred to as strategic planning, performance management, program evaluation, or performance budgeting, to inform management decisions for program and policy officials. These efforts have contributed to significant investments being made in the development of an evidence base for effective programs. However, comparing the effectiveness of programs has proven more elusive, and looking at system-wide cost effectiveness is rare. Research studies in addition to private and public-sector analyses may be of value to Federal efforts to develop and implement cost-benefit evaluations. For example, the Washington State Institute for Public Policy maintains a list of available, evidence-based public policy options and ranks them by return on investment.[127] While not a complete list, such ranked lists provide policymakers with a better understanding of the likelihood of which, of the many policy options available, are most likely to produce more benefits at lower costs.

Given the substantial challenges of the heroin and prescription opioid epidemic, it is critically important that the Federal Government maximize the impact of its response by supporting the most effective programs and policies to reduce the number of individuals affected by OUDs and end the nation's opioid epidemic. A thorough review of programs and policy options would assist the Director of ONDCP in making recommendations on how to best allocate scarce federal resources to achieve the objectives of the *National Drug Control Strategy*.

3. **To achieve accountability in federal programs, the Commission recommends that ONDCP review is a component of every federal program and that necessary funding is provided for implementation. Cooperation by federal agencies and the states must be mandated.**

Opioid Addiction Prevention

It is important to consider that the national crisis is not only about prescription or illicit opioids. We are focusing on this class of substances, but prevention efforts need to be broader because the removal of one substance conceivably will be replaced with another.

To address the opioid and addiction epidemic, it is vital to make substance use and misuse prevention a much higher priority and stop the pipeline into addiction. In the first Commission meeting, General Arthur Dean, speaking on behalf of Community Anti-Drug Coalitions of America, expressed the strong belief that prevention has been underutilized, relative to its importance and cost-effectiveness in preventing or reducing drug use and misuse and the related human and societal costs. The American Society of Addiction Medicine (ASAM) and the Addiction Policy Forum both recommended the launch of a national public education campaign, similar to the one developed for the AIDS epidemic in the 1980s, to raise awareness that addiction is not a moral failing, but rather a chronic brain disease, and that evidence-based treatment is available.

A generalized prevention campaign should address use of illicit drugs with abuse potential, as they can progress to addiction. Addiction is the most prevalent and costliest of neuropsychiatric disorders and the leading cause of premature, preventable deaths and disability in the United States. Of the ~2 million annual deaths in the United States, one-quarter are attributable to the consequences of tobacco, alcohol, opioids, and other drugs. Drugs impact every sector of society – individuals, families, communities, healthcare systems, educational environment, workplace, traffic safety, and the criminal justice system. Studies investigating the effects of drugs in the brain, body, and on behavior has yielded a vast base of information over the past twenty years, relevant and indeed critical information for public education. These research discoveries have outsized power and potential to heighten awareness and promote prevention, but their impact has been limited by discontinuities in translating research into effective prevention messages and broadcasting them widely. The current opioid crisis dramatically illustrates an unfulfilled need for expanded educational outreach to new generations of youth, their parents and the general population. Youth are more susceptible to addiction and are a key target cohort for prevention. The vast majority of users fall into 16-34 age category, a peak period for pregnancy, parenting, and for adverse consequences of drugs: addiction, underemployment, health issues, accidents, and trauma. It is well recognized that use rates are inversely correlated with perception of risk, yet effective state-of-the-art, credible, compelling, and comprehensible information on the risks and adverse health consequences of drugs has not been mounted to reverse these trends.

The National Institute on Drug Abuse's (NIDA) Drug Facts Chat Day website (http://drugfactsweek.drugabuse.gov/chat/) offers some insights into young people's curiosity for accurate information about drugs and the lack of accessibility to information. Teenagers from around the nation are offered a day-long session to ask NIDA staff their personal question about drugs. A sampling of questions is listed below:

- What is in drugs that make it so addictive?
- What should you do if a parent is doing drugs?
- Do drugs kill brain cells?
- Is drinking worse than smoking?

During this nation's worst drug crisis, there is no more opportune time to launch a national prevention campaign that highlights the hazards of substance use, but also focuses on the opioid crisis: (1) to educate the public on risks and consequences of drug use in general, with emphasis on opioids; (2) to focus on the vulnerable - adolescents, college age students, pregnant women, those harboring a psychiatric disorder, and the elderly - and highlight the detrimental effects of opioids; (3) to convey to parents their critical role in determining their children's use of drugs; (4) to show parents how to engage in crucial conversations with children about drugs; (5) to dispel common myths and misinformation on drugs; (6) to educate families on warning signs in family members and on reducing environmental risks for children; (7) to advance the concept of addiction as a treatable brain disease; and (8) to tailor messages to specific populations and communities in need. Many sources of information exist from government agencies (e.g. NIDA, SAMHSA, National Institute on Alcohol Abuse and Alcoholism [NIAAA], DEA) or on websites of non- and for-profit private organizations. The reach of these websites is limited, and their impact and value undetermined. Creative strategies are needed to engage much larger populations, with accountability on effectiveness.

Notably, recent surveys indicate that parents can be key contributors to a child's use or non-use of drugs**.** Youth alcohol or marijuana use was 5-7-fold lower if parents took a strong stance against use, compared with parents whose views were ambivalent. Systematic reviews have reinforced this conclusion.[128,129] Yet, parental knowledge is limited, as illustrated by examples from a recent survey:

a) Nine of ten parents do not think that teens spending time on social networking sites like Facebook are likelier to drink or use drugs. Yet, teens who spend time on a social networking site in a typical day are much likelier to use tobacco, alcohol, and other drugs than teens who don't spend time on a social networking site in a typical day; [130]

b) When asked, "do you consider it necessary to take steps to keep your child from having access to prescriptions for painkillers such as Oxycontin, Vicodin or Percocet in your home?," 57% of parents with prescription pain killers in their home did not consider it necessary to prevent their child from accessing the prescriptions,[131] even though more than 50% of people who misuse prescription pain killers obtained them for free from friends and family.[132] Yet, the 2016 national survey indicates that parental attitudes are critical in determining youth drug use.[133]

c) One-third of parents surveyed reported that it was "very likely" or "somewhat likely" that their teen would "try drugs (including marijuana or prescription drugs without a prescription to get high) at some point in the future." Yet, if parents are perceived to disapprove of marijuana use, use among youth is approximately 9 times lower. [134]

Parents have been under-represented in prevention programs, even though evidence is robust that parent-based prevention programs can play a pivotal role in delaying the onset and use of alcohol and other drugs, an influence that persists during adolescent development. Furthermore, universal prevention programs are enhanced with inclusion of parent-based components.[135] In a systematic review of studies which combined student- and parent-based programs to prevent or reduce adolescent alcohol, tobacco or marijuana use, effectiveness was shown in the majority of studies.

In summary, there is a compelling need to integrate evidence-based prevention programs in large scale outreach programs within schools. With tools for teachers and parents to enhance youth knowledge of the dangers of drug use, early intervention strategies can be implemented for

children with environmental and individual risk factors (trauma, foster care, adverse childhood experiences [ACEs], and developmental disorders).

Evidence-based Prevention Programs

Substance abuse prevention is a process which requires a shift in behavior, culture, and community norms. An investment in prevention requires meaningful outcome measures planned in coordination with the program. Demonstrated evidence of program effectiveness can include delaying the age of initiation of substance use, decreasing the number of new or current users, decreasing the frequency of use, reducing the adverse consequences of use (e.g. effect on school grades, employment, and others), decreasing use among contacts,[136] and duration of effect. When evidence-based programs are selected for specific populations and implemented with fidelity, they can be effective. Prevention programs need to be tested for scalability, fidelity, and sustainability after research champions are no longer present to drive programs. Prevention is most successful when messages are consistent, culturally-appropriate, repeated at home, reinforced in schools, workplaces, and community organizations, and delivered by influential adults and peers.

NASEM has described three categories of prevention interventions: universal, selective, and indicated. These interventions have been researched based on targeted populations and risk factors (e.g. schools, parents, or youth). Risk and protective factors are influential at different times during development, and they relate to changes that occur over the course of development. Risk factors can interrupt developmental patterns and it is therefore important to implement programs designed for early developmental periods by building on the strengths of the child or caregiver. Intervening early in childhood can alter the life course trajectory in a positive direction.[137]

Below is a description of the three categories of prevention interventions that target several risk factors and increase protective factors:

- Universal interventions attempt to reduce specific health problems across all people in a particular population by reducing a variety of risk factors and promoting a broad range of protective factors. Examples of universal programs include:
  - Good Behavior Game[138]
  - Nurse Family Partnership[139,140]
  - Life Skills Training (LST)[141]
  - Strengthening Families Program 10-14[142]
  - Communities that Care[143]
- Selective interventions are delivered to particular communities, families, or children who, due to their exposure to risk factors, are at increased risk of substance misuse problems. Selective interventions may include families living in poverty, the children of depressed or substance using parents, and children who have difficulties with social skills or may have experienced trauma. Examples of selective programs include:
  - Coping Power[144]
  - Focus on Families[145]

- Indicated interventions are directed to those who are already involved in a risky behavior, such as substance misuse, or are beginning to have problems, but who have not yet developed an SUD. Examples of individual intervention programs include:
  - Project Toward No Drug Abuse
  - BASICS
  - Keepin' it Real

School programs implementing environmental approaches targeting children focus on building a repertoire of positive competencies, including in the areas of academics, self-regulation, and social skills. Teachers can focus on interventions in the classroom for those who may need support with self-regulation and social skills. Increasing the capacity of teachers by training them in classroom management strategies (e.g. establishing clear rules and rewards for compliance, teaching interactively, and promoting cooperative learning) provides them with the skills for managing behaviors and teaching children self-regulation.[146] Risk and protective factors can be influenced by the choice of programs and policies at multiple levels, including federal, state, community, family, school, and the individual.

One advantage of a properly implemented universal prevention intervention is that it is likely to reach most or all the population (e.g. school-based interventions are likely to reach all students). Targeted (selective and indicated) approaches provide more intensive services to those who are reached. It is prudent for communities to provide a mix of universal, selective, and indicated preventive interventions.[147]

SBIRT as a School Prevention Strategy

SBIRT is an evidence-based systematic method to screen for problematic use of all substances and, depending on a cumulative score, follow up with a brief intervention or referral to specialty treatment. The service was catapulted more widely into healthcare systems following a report from the Federal Government demonstrating effectiveness in reducing substance use,[148] and the advent of billing codes to reimburse for these services.[149] Although traditionally developed for clinical care, SBIRT services have been increasingly offered in high schools and universities. School nurses and counselors are uniquely positioned to discuss substance use among young people.

In 2016, Massachusetts passed a bill enabling appropriately trained staff to reinforce prevention, screen for substance use, provide counseling and make referrals as necessary to all adolescents, including students in upper elementary grades. Adolescent SBIRT focuses on prevention, early detection, risk assessment, brief counseling and referral intervention that can be utilized in the school setting. Use of a validated screening tool (CRAFFT) focused on adolescents has enabled school nurses and counselors to detect risk for substance use-related problems and to address them at an early stage in adolescents. The bill requires all public-school districts in Massachusetts to screen seventh and 10th graders for potential drug use, and is viewed as a way to interrupt the potential use of drugs, including opioids, at an early stage. The screenings do not involve drug tests, but rather a screener (school nurse or psychologist trained in conversations on drug use with youth) to determine through a conversation/questionnaire if the student is engaged in risky substance use. The intent is to identify students who need help and to try to motivate them into treatment. Students or parents can opt out of the screening and parents are not immediately notified of the screening results to protect students' privacy. Parents are notified only in severe cases of addiction.

Previous research showed that 14.8% of adolescents had positive results on the CRAFFT screen. Prevalence rates differed significantly across practices after adjusting for demographic factors. The highest positive rates on the CRAFFT screen were at school-based health centers (29.5%) and the rural family practice (24.2%), the middle rate was at the adolescent clinic (16.6%), and lowest rates were at the health maintenance organization (14.1%) and pediatric clinic (8.0%). Sick visits had the highest rate (23.2%). Well-child care visits had a significantly lower rate (11.4%). Statistical modeling estimated that 11.3% of all patients had problematic use, 7.1% reported abuse, and 3.2% had an SUD. Substance abuse screening should occur whenever feasible, and not only at well-child care visits.[150] Recently the State of New Mexico has begun a program for universal screening,[151] the State of New York has initiated SBIRT trials,[152] and calls for universal screening using validated SBIRT screening tools are increasing.[153]

Ohio State University developed an SBIRT course with the goal of making SBIRT accessible for use on college and university campuses nationwide. To meet this goal, the Higher Education Center for Alcohol Drug Misuse Prevention and Recovery developed ScreenU, a web-based program that allows SBIRT to be implemented with college students either independently or together with a campus professional. ScreenU identifies students who are misusing alcohol or prescription drugs and provides feedback and strategies to reduce their risk for experiencing negative consequences from their use.

4. The Commission recommends that Department of Education (DOE) collaborate with states on student assessment programs such as Screening, Brief Intervention and Referral to Treatment (SBIRT). SBIRT is a program that uses a screening tool by trained staff to identify at-risk youth who may need treatment. This should be deployed for adolescents in middle school, high school and college levels. This is a significant prevention tool.

Mass Media Public Education Campaigns

Mass-media campaigns are one of the primary universal prevention strategies for delivering educational messages on health promotion to youth and adults. A review of the literature provides an overview of the lessons learned from research on mass-media campaigns. The literature is quite clear that mass media campaigns can increase awareness of messages but are not always successful in changing attitudes, beliefs, or behaviors.[154] Mass-media campaigns tend to work best when they are well-targeted and supported by comprehensive community-based efforts that coordinate clinical, regulatory, economic, and social strategies. In addition, funding for local prevention interventions that prevent initiation of a behavior and treatment programs that promote abstinence and recovery are important.

In addition to policies and strategies that help create environments that are less conducive to substance use, mass media campaigns can focus on either directly influencing individual level predictors or influencing an individual's behavior through targeting others within youths' social environment. The former strategy looks to increase knowledge about a particular drug, its negative health effects, self-efficacy in declining or stopping use, beliefs about the drug, and social norms about licit and illicit drug use. The latter includes messages which discourage young people from pressuring friends to use.[155]

Regardless of the approach, for a mass-media campaign to be effective, it is critical to develop coherent, credible, evidence based-messages that are grounded in behavioral science.[156] This is critical to counteract the meta-messaging that drug use in society is pervasive and normal.[157] Media messaging also must strategically target populations with culturally appropriate messages, take advantage of multiple media platforms, and have sufficient resources to provide broad exposure over a significant period of time to ensure an effect. Branding the campaign also has been shown to enhance the impact of public health messaging as has integrating a media literacy component that helps train youth and young adults to critically view messages about substance use, be they within television shows, movies, or advertising.

The literature is very limited on mass-media campaigns focusing on prescription opioids, and even less on heroin and other opioids. There is a more robust literature on lessons learned from mass-media prevention campaigns on alcohol and tobacco, which have been incorporated.

ONDCP's earlier paid advertising campaign, the *National Youth Anti-Drug Media Campaign*, targeted young people aged 9 to 18 years, their parents, and other influential adults. It used a combination of television, radio advertising, other media, and community programming with the goals to educate and enable youth to reject illegal drugs, prevent youth from initiating use of drugs, especially marijuana and inhalants, and convince occasional users of marijuana and other drugs to stop using. A comprehensive evaluation of the campaign[158] found substantial evidence that the campaign favorably impacted parents on measures such as thinking about and talking with their children about drugs, doing fun activities with their children, and beliefs about monitoring their children, but found little favorable direct effects of the campaign on youth. The evaluation found there were significant delayed unfavorable effects of exposure to the campaign on social norms and perceptions of use by youth; greater exposure was associated with weaker anti-drug norms. Additionally, greater exposure may have led to higher rates of initiation of marijuana use. Also, there was no evidence found to suggest that higher exposure to the campaign had any impact on quitting or reducing use.

Governor Otter shared with the Commission Chair the successes of the Idaho *Meth Project*, a large-scale prevention program founded in 2005 with the aim to reduce methamphetamine use through a comprehensive approach including public services messages, public policy approaches, community outreach, and in-school lessons. *The Meth Project* reports that 94% of teens that are aware of the anti-meth campaign ads say they make them less likely to try or use meth, and that Idaho has experienced a 56% decline in teen meth use since the campaign began in 2007. In a pooled analysis of sites, including from Colorado, Georgia, Hawaii, Idaho, Montana and Wyoming, no evidence was found of change in past month use among subjects aged 12-17.[159] However, there was evidence of reduction in past year use among this age group. In Idaho, this initiative was re-branded in 2016 as the *Idaho Prevention Project* to include opioids and prescription drugs.

Another study evaluated the impact of the SENsation seeking TARgeting approach (*SENTAR*) focusing on anti-heroin public service announcements (PSAs) on processing, affect, and anti-heroin attitudes in a sample of 200 young adults.[160] Building on previous work,[161] this study recruited subjects from communications courses at a large Midwestern University exposing them to 30-second anti-heroin PSAs selected from a larger pool of PSAs produced by the Partnership for a Drug Free America. It utilized data from the 5-year television-based media campaign using public service announcements targeting messages. They found that high-sensation seekers' anti-

heroin attitudes were largely influenced by narrative and sensory processes and low sensation seekers' anti-heroin attitudes were relatively unaffected by anti-heroin ads.

A national education campaign focused on opioids could be modelled after *The Real Cost*, an existing award-winning youth tobacco prevention campaign from the FDA. *The Real Cost* seeks to educate at-risk teens about the harmful effects of tobacco use with the goal of preventing youth who are open to using tobacco from trying it and reducing the number of youth who move from experimenting with tobacco to regular use. It was launched nationally in February 2014 across multiple media platforms including TV, radio, print, web, social media, and out-of-home sites, like billboards. Initial campaign advertising focused on reaching the nearly 10 million youth ages 12-17 in the United States who are either open to trying smoking or are already experimenting with cigarettes. Results from the first evaluation published in 2015 indicated that 9 out of 10 youth reported seeing *The Real Cost* ads seven months after the campaign launch and that the campaign positively affected tobacco-related risk perceptions and beliefs after 15 months. Further, from 2014-2016, the campaign was associated with a 30% decrease in the risk of smoking initiation which translates into preventing an estimated 350,000 youths aged 11-18 from smoking.[162]

Media Campaign Focusing on Opioids

A national prevention strategy with a comprehensive public health mass media campaign supported by evidence-based prevention programs is timely and essential. The goals would include: (a) universal drug prevention messages, as current or past SUDs predispose individuals to misusing opioids, and polysubstance use disorders are common; (b) youth-directed messages, as they are more susceptible to addiction and other adverse consequences; (c) prevention messages specific to opioids, to include patient and family education on what opioids are, the hazards of opioids, safeguarding of prescription medications, and disposing of unused pills; (d) the common hazards of illicit and prescription opioids; and (e) availability of treatment resources. Media campaigns are commonly used to deliver preventive health messages and to shape healthy behaviors and attitudes. There are several successful state, local government and grassroots media campaigns aimed at providing drug-related public education or assistance in locating appropriate help for children. During the first Commission meeting on June 16, 2017, the Commission heard about one such campaign from the Partnership for Drug-Free Kids, who have worked with national and local media partners, as well as private sector partners like Google and Facebook, to run public service announcements that inform parents on available help for their loved ones. Similarly, Commission Chairman Governor Christie has implemented a media campaign in New Jersey around opioid addiction and a help hotline and website.

A comprehensive public health mass media campaign should be conceived carefully, pilot tested on target audiences, quantitative goals established, and outcomes measured that are matched to goals. Initially, accurate, anonymous, and actionable national data can be collected by probing the internet about the opioid crisis and, more broadly, youth attitudes towards drugs. Data analytical industries are capable of uncovering the extent, locations, spread, who are most affected by specific drugs being used, and how they are obtained by surveying the web in real-time with keywords.[163] These probes can also identify treatment barriers, including shame, stigma, mistrust, cost, service availability, service preference, treatment avoidance, perceptions of service quality, and denial of service. Probes and interactive dashboards can scientifically test the potential success of public health video and other multi-media messaging on anti-drug campaigns, and shifts in sentiments, opinions, to provide continuous real-time survey data.

Since use of specific drugs is initiated in different age ranges, the campaign would need to be shaped according to various demographics. For example, alcohol, tobacco, marijuana, and inhalant use begins, on average, in early adolescence; the use of cocaine, methamphetamine, and hallucinogens in the later teen years; the misuse of prescription drugs (e.g., stimulants, tranquilizers, barbiturates, and pain relievers) and illicit opioids typically begins in early adulthood.

There is an unmet need to launch a portfolio of *comprehensible, compelling,* and *universal* information to educate our nation on drug-related vulnerabilities of youth and other populations. Audiences would include teens, parents, people with psychiatric disorders, older adults, and pregnant women. Information would be created for television and for the internet, with a portfolio of animated, visual, interactive, narrated material, or videos, with minimal text, and pop-ups to counter misinformation on drug. This form of communication has the advantage of fidelity, interactivity, feedback, and sustainability.[164] It can be dispersed on social networking sites, accessible via computers, iPad, smartphones or smartwatches. The internet is rapidly evolving as the most important medium for teens, where teen beliefs and perceptions are shaped, strengthened, and shared. Web-based digital, interactive, narrated, and animated materials should focus on: (a) the hazards of opioid use; (b) the risks of adolescent drug use; (c) the risks of opioid use during pregnancy; (d) the crucial role of parents in protecting children; (e) counter common myths and misinformation on drugs; and (f) educating youth and parents on signs of an emerging SUD. As mentioned above, parents can be major influencers on a child's use or non-use of drugs, as drug use is considerably lower among youth if parents deliver strong, clear messages disapproving of drug use, are involved with their children's school work, set clear limits on children's behavior by monitoring their time, friends, and supervising activities, and communicate and connect effectively with their children.

The media campaign's messaging will need to be amplified and extended by the integrative efforts of evidence-based prevention programs at the local level, many of which receive support from the Federal Government. To achieve the desired ultimate outcome — reduction in drug use — the campaign needs the support of locally implemented evidence-based prevention programming. The campaign's messaging needs to be integrated closely with local efforts and amplified by them. Local partners could include community coalitions, such as ONDCP's Drug-Free Community grantees, schools, hospitals, law enforcement, businesses, religious institutions, and local government. In this way, strong anti-drug abuse messages tightly focused on targeted audiences would serve to raise awareness of the problem and solutions to it and improve anti-drug attitudes, beliefs and intentions, driving parents, adult influencers and youth to the local evidence-based prevention resources available to achieve the desired behavioral outcomes.

Although the funding level for the recommended campaign has not yet been determined, the initial funding request in FY 1998 for the National Youth Anti-Drug Media Campaign was $200 million per year. Those entities receiving campaign funds to air/print its messages were required to match the funds received, thus doubling the purchasing power of the federal funds. The Commission believes that a coordinated media campaign that can be rolled out nationally with a consistent message about the dangers of both illicit and prescription drugs, including opioids could effectively educate youth, parents, pregnant women, remove stigma associated with the disease of addiction, and reduce drug use and misuse.

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5. The Commission recommends the Administration fund and collaborate with private sector and non-profit partners to design and implement a wide-reaching, national multi-

platform media campaign addressing the hazards of substance use, the danger of opioids, and stigma. A similar mass media/educational campaign was launched during the AIDs public health crisis.

Opioid Prescription Practices

More than 20 years ago, a growing compulsion to detect and treat pain set in motion the prescribing of opioids beyond traditional boundaries of treating acute, postoperative, and procedural pain and end-of-life care. The surge in opioid supply escalated into opioid-related misuse, diversion, use disorder, overdose deaths, and the advent of deadly fentanyl analogs. One of the areas which can have the greatest impact in the opioid crisis is reducing the rate of new addictions. This can be partly accomplished by aiming to prescribe opioids to appropriately indicated patients, and that prescription durations and doses match the clinical reason for which the drug is prescribed. Some states have set firm limits on the maximum number of days of prescribed opioids at initial encounters, irrespective of pain condition.

Improving upon the CDC *Guideline for Prescribing Opioids for Chronic Pain* and Provider/Prescriber Education

In March of 2016, the CDC developed and published a guideline for prescribing opioid pain medications for adults 18 years of age and older in *primary care settings*.[165] This guideline is "intended to improve the communication between provider and patient about the risks and benefits of opioid therapy for chronic pain, improve treatment safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including OUD and overdose." The guideline focuses on three key areas: 1) determining when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up and discontinuation; and 3) assessing risk and addressing harms of opioid use. Prescriptions by primary care clinicians account for nearly half of all dispensed opioid prescriptions, and the growth in prescribing rates among these clinicians have been above average. More importantly, use of prescription opioids for more than 90 days increases the risk of progression towards addiction.[166] A CDC "Morbidity and Mortality Weekly Report" published in July 2017 found that while prescriptions for opioid medications have decreased since 2010, substantial variation in opioid prescribing was observed at the county-level across the U.S.,[167] demonstrating "the need for better application of guidance and standards around opioid prescribing practices."

In the first Commission meeting, the Commission heard from various medical societies about the need to promote expanded implementation of the CDC opioid prescribing guideline. However, while many professional organizations encourage use of the CDC guideline, it is important to note the Commission received a substantial amount of correspondence from patients who currently use opioid medications for legitimate medical reasons and are worried about the guideline being too restrictive for their physicians to properly treat them. Clinicians have added their concerns about the CDC guideline, including the time required to discuss alternative forms of pain control, the difficulty in obtaining reimbursement for alternatives, how to address opioid tapering, and concerns with the prescribing guideline for specific forms of pain. Furthermore, it is important to point out that the CDC guideline is intended for *primary care clinicians*, who are treating patients

for chronic pain in outpatient settings, and more latitude in decision making should be given to physicians that have specialized training in pain management. The Commission also recognizes that the CDC guideline may not include specific recommendations regarding patient education and informed consent.[168] Patients are often ill-informed about the risks of taking opioid analgesics and, therefore, are not able to balance the potential benefits of opioid analgesics with the associated risks.

While progress has been made in training prescribers and fostering the adoption of prescribing guidelines such as the CDC guideline, the Commission has learned that not all states have adopted the guideline, not all physicians are aware of them, and sound opioid prescribing guidelines are far from universally followed. For example, while the CDC guideline, as well as guidelines from the VA and the Department of Defense (DOD), recommend clinicians use baseline and periodic urine testing as part of a comprehensive plan to ensure the safe and effective use of opioid therapies, not all states have placed sufficient emphasis upon the utility of medication screenings. In the current crisis, drug testing not only allows providers to assess proper use of prescribed medications in individual patients, but it would also be part of a broader solution in fighting the opioid crisis, as it can provide a snapshot of controlled prescription drugs and illicit drugs available in a community.

Consequently, the Commission recommended in the interim report that medical education and prescriber education initiatives in proper opioid prescribing and risks of developing an SUD be mandated (Appendix 3).

Stakeholders important to the adoption of prescribing guidelines include public and private payers, medical and dental schools, physician and pharmacy groups, insurers, and health care associations. Medical associations have developed courses for proper opioid prescribing practices, with support from federal grants and made them available online for free.[169,170,171,172] Federal agencies have also compiled lists of courses in compliance with the CDC guideline.[173,174] It is imperative that all DEA registrants prescribing scheduled drugs develop proficiency in pain management and opioid prescribing. In recognizing that OUD is associated with or preceded by other SUDs, training on diagnosis and office-based treatment of addictions should also be implemented for all stages of professional activity, including medical school, residency, practicing clinicians, and all others legally permitted to prescribe scheduled drugs.

Given that the practice of medicine, including prescribing, is regulated primarily at the state level, strategies for ensuring that prescribers are better informed and that patients are educated about the relative risks and benefits of opioid analgesics should incorporate state governments. Many states have acted to improve the safety of opioid prescribing. In July 2016, for example, 45 state governors signed the *Compact to Fight Opioid Addiction*[175] under which signatories agreed to update prescribing guidelines, require pain management continuing education for prescribers, improve monitoring of providers prescribing opioids, and increase access to treatment and recovery support services through state healthcare programs.[176] In March 2016, Massachusetts passed legislation[177] limiting opioid analgesic prescriptions to a seven-day supply for first-time adult users and for minors, mandating continuing medical education (CME) credits for effective pain management, and requiring prescribers to check the state PDMP before writing a prescription for a Schedule II or Schedule III narcotic.

Since January 2012, the State of Washington has required written treatment plans for use of opioid analgesics and a written agreement between patients and prescribers outlining patient responsibilities, including: taking the medications as prescribed; providing biological samples for

toxicology testing; releasing the agreement for treatment to local EDs, urgent care facilities, and pharmacies; authorizing the prescriber to notify authorities if there is reason to believe the patient has engaged in illegal activities; and, acknowledging that it is the patient's responsibility to safeguard all medications and keep them in a secure location.[178]

A recent survey in Massachusetts found that 50% of respondents felt that painkillers are prescribed too often or in larger doses than necessary; 47% felt that getting painkillers from those who save them is too easy. Only 36% of respondents who had been prescribed an opioid were informed of the addiction potential by their prescriber either before or while they were taking the medication.[179] In 2014, 4.4 million prescriptions for Schedule II or Schedule III opioids were written for Massachusetts residents, resulting in the dispensation of 240 million pills or tablets.[180] Together, these data point to the need to explore prescriber and patient education as a component of any strategy to address the current opioid epidemic. A review of the curricula at the four medical schools in Massachusetts revealed that, although they taught components of addiction medicine, no uniform standard existed to ensure that all students were taught prevention and management strategies for prescription drug misuse.

To fill this gap, Commission member Governor Baker and the Massachusetts Secretary of Health and Human Services invited the deans of the state's four medical schools to convene to develop a common educational strategy for teaching safe and effective opioid-prescribing practices. With leadership from the Department of Public Health and Massachusetts Medical Society, the deans formed the Medical Education Working Group in 2015. This group reviewed the relevant literature and current standards for treating SUDs and defined 10 core competencies for the prevention and management of prescription drug misuse. The medical schools have incorporated these competencies into their curricula and have committed to assessing students' competence in these areas. The members of the Medical Education Working Group have agreed to continue to work together on key next steps, including connecting these competencies to those for residents, equipping inter-professional teams to address prescription drug misuse, and developing materials in pain management and opioid misuse for practicing physicians. This first-in-the-nation partnership has yielded cross-institutional competencies that aim to address a public health emergency in real time.

The following themes emerged from a literature review and from national and local standards for treating SUDs. The core competencies are meant to enhance medical student training in primary, secondary, and tertiary prevention strategies for prescription drug misuse and to provide students with a strong foundation in prevention, identifying SUDs, and referring patients to appropriate treatment. These competencies are designed to serve as a vital bridge between undergraduate medical education and residency training.

1. Evaluate a patient's pain using age, gender, and culturally appropriate evidence-based methodologies.
2. Evaluate a patient's risk for SUDs by using age, gender, and culturally appropriate evidence-based communication skills and assessment methodologies, supplemented by relevant available patient information, including but not limited to health records, prescription dispensing records (e.g., the Prescription Drug Monitoring Program), drug urine screenings, and screenings for commonly co-occurring psychiatric disorders (especially depression, anxiety disorders, and posttraumatic stress disorder).
3. Identify and describe potential pharmacological and nonpharmacological treatment options, including opioid and nonopioid pharmacological treatments for acute and chronic

pain management, along with patient communication and education regarding the risks and benefits associated with each of these available treatment options.

- Secondary prevention domain: Treating patients at risk for SUDs (engaging patients in safe, informed, and patient-centered treatment planning)

4. Describe SUD treatment options, including MAT, as well as demonstrate the ability to appropriately refer patients to addiction medicine specialists and treatment programs for both relapse prevention and co-occurring psychiatric disorders.
5. Prepare evidence-based and patient-centered pain management and SUD treatment plans for patients with acute and chronic pain with special attention to safe prescribing and recognizing patients displaying signs of aberrant prescription use behaviors.
6. Demonstrate the foundational skills in patient-centered counseling and behavior change in the context of a patient encounter, consistent with evidence-based techniques.

- Tertiary prevention domain: Managing SUDs as chronic diseases (eliminating stigma and building awareness of social determinants)

7. Recognize the risk factors for, and signs of, opioid overdose and demonstrate the correct use of naloxone rescue.
8. Recognize SUDs as a chronic disease by effectively applying a chronic disease model in the ongoing assessment and management of the patient.
9. Recognize their own and societal stigmatization and biases against individuals with SUDs and associated evidence-based MAT
10. Identify and incorporate relevant data regarding social determinants of health into treatment planning for SUDs.

Integrating the core competencies for the prevention and management of prescription drug misuse with any related competencies for residents is critical to ensuring that medical students are required to maintain and expand these skills as they enter residency training. Furthermore, the group recognized the need to expand inter-professional education opportunities designed to better equip collaborative teams for primary, secondary, and tertiary prevention of OUDs. As other practitioners, including nurses, pharmacists, dentists, and mental health providers, among others, also contribute to the provision of care, they too must demonstrate competence in this area. Finally, the group recognized the need for continuing medical education materials for current prescribers.

The level of urgency is greater than ever to develop creative solutions based on exploiting modern data mining and communication proficiencies. A more rational approach is to develop detailed and specific guidance for clinicians treating specific manifestations of pain. With modern data analytical techniques capable of interrogating vast prescribing databases, it is feasible to identify current patterns of opioid prescribing for specific conditions, recommend changes in practice patterns based on specific pain sources and medical specialties, and create active programs to educate practitioners on these recommendations. Combined with data from PDMPs, a simple electronic printout conceivably can assist in guiding a physician's decision on prescribing opioids or alternatives for pain management. Decisions on pain management can be fortified with additional information on a patient's physical and mental health status, as the complex causes of pain can arise from a confluence of biological, psychological, and social factors.

To advance this goal, providers need to be informed about suitable prescribing practices for opioids, a class of drugs which confer benefit, as well as high risk. Pharmacoepidemiology

research can facilitate improvements to the CDC guideline by initially defining existing patterns of opioid use and then developing condition-specific guidelines on optimal opioid dosing.[181,182]

To create a more useful foundation for interventions to reduce improper use of prescription opioids, much more needs to be known of existing patterns of prescription for specific conditions, including diagnosis, drug choice, dose, amount prescribed, and physician and patient characteristics. This work would draw on the extensive experience of pharmacoepidemiological analysis,[183] as well as extensive population-based datasets from both the public and private sector.[184] These studies will help to define which specific problems of opioid overuse are most prevalent in which settings in order to better focus public and private interventions on the areas of greatest need, in terms of clinical conditions, provider types, patient characteristics, and practice settings. The second and more important goal is to develop condition-specific guidelines on optimal opioid dosing. While CDC and other groups have set forth general guidelines on the principles of pain management, and some states have established uniform limits on the maximum number of tablets or capsules that can be prescribed for a first opioid prescription, clinicians need more detailed and specific guidance on drug choice, dose, and quantity to be dispensed in treating specific common conditions. Data analytics can build on the overall guidance documents prepared for pain management in general by: (a) reviewing the entire existing literature on evidence concerning condition-specific pain therapy, including recommended agents, doses, and quantities; (b) convening several expert clinician panels to generate condition-specific guidelines for managing the most common indications for pain medications; and (c) transforming that information into concise, clinically relevant, and actionable recommendations that can be disseminated to practitioners.

Pharmacists are under pressure to continue filling prescriptions from irresponsible providers. A recent study of Wisconsin pharmacists found that a not insignificant minority did not understand what is legitimate practice under federal and state laws about evaluating the legitimacy of a controlled substance prescription – also known as corresponding responsibility. Further, 36% of these pharmacists considered extended prescribing of opioids to be a violation of law or unacceptable medical practice. In the current crisis, it is critical that all pharmacists and pharmacy programs have the training necessary to responsibly dispense these medications while also not dispensing these powerful medications when the prescription is not legitimate or if it will harm the patient.[185]

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6. **The Commission recommends HHS, the Department of Labor (DOL), VA/DOD, FDA, and ONDCP work with stakeholders to develop model statutes, regulations, and policies that ensure informed patient consent prior to an opioid prescription for chronic pain. Patients need to understand the risks, benefits and alternatives to taking opioids. This is not the standard today.**

7. **The Commission recommends that HHS coordinate the development of a national curriculum and standard of care for opioid prescribers. An updated set of guidelines for prescription pain medications should be established by an expert committee composed of various specialty practices to supplement the CDC guideline that are specifically targeted to primary care physicians.**

8. **The Commission recommends that federal agencies work to collect participation data. Data on prescribing patterns should be matched with participation in continuing medical**

education data to determine program effectiveness and such analytics shared with clinicians and stakeholders such as state licensing boards.

9. **The Commission recommends that the Administration develop a model training program to be disseminated to all levels of medical education (including all prescribers) on screening for substance use and mental health status to identify at risk patients.**

10. **The Commission recommends the Administration work with Congress to amend the Controlled Substances Act to allow the DEA to require that all prescribers desiring to be relicensed to prescribe opioids show participation in an approved continuing medical education program on opioid prescribing.**

11. **The Commission recommends that HHS, DOJ/DEA, ONDCP, and pharmacy associations train pharmacists on best practices to evaluate legitimacy of opioid prescriptions, and not penalize pharmacists for denying inappropriate prescriptions.**

Enhancing Prescription Drug Monitoring Programs (PDMP)

State-based PDMPs are electronic databases that give prescribers and many pharmacists access to critical information regarding a patient's controlled substance prescription history, and which can help health professionals identify patients who may be misusing prescription opioids or other prescription drugs and who may be at risk for abuse or misuse. PDMPs are sometimes used by professional licensing boards to identify clinicians with patterns of inappropriate prescribing and dispensing. In most states, law enforcement may use them to investigate cases of controlled substance diversion. In the interim report, the Commission recommended that federal funding and technical support be provided to states to enhance data sharing among PDMPs to better track patient-specific prescription data and support regional law enforcement in cases of controlled substance diversion (Appendix 3). The commission believes the additional recommendations outlined below will further enhance the effectiveness and uptake of PDMPs across the nation.

Today, 49 states and the District of Columbia currently have legislation authorizing the operation of PDMPs in their jurisdictions. However, except in states with mandated PDMP use, providers who see patients and prescribe opioids, or have patients affected by opioids, don't routinely register for or use PDMPs. The national median PDMP registration rate among licensed prescribers is only 35%, per a report in the Journal of the American Medical Association published in 2015. Furthermore, a study by the Johns Hopkins Bloomberg School of Public Health found that patient history was not checked via a PDMP database by the prescriber in 86% of prescriptions for opioids written in 2015.

The Federal Government should leverage mechanisms to facilitate PDMP use. Congress should pass and the President should sign the Prescription Drug Monitoring (PDMP) Act of 2017, which would mandate the creation and use of PDMPs by states who receive federal funding to fight the opioid crisis. This Act would impose strict PDMP requirements, such as a 24-hour reporting requirement after dispensing a controlled substance, further centralize prescribing data, and would help to facilitate data sharing across the states.

12. **The Commission recommends the Administration's support of the Prescription Drug Monitoring (PDMP) Act to mandate states that receive grant funds to comply with PDMP**

requirements, including data sharing. This Act directs DOJ to fund the establishment and maintenance of a data-sharing hub.

13. **The Commission recommends federal agencies mandate PDMP checks, and consider amending requirements under the Emergency Medical Treatment and Labor Act (EMTALA), which requires hospitals to screen and stabilize patients in an emergency department, regardless of insurance status or ability to pay.**

Providers often resist using PDMPs because these systems are not well integrated into the electronic health records (EHR) systems they currently use in practice, and for other reasons, including inadequate training on the use and complexity of some PDMP software programs. The Heller School at Brandeis University recommends simplifying the method of access to PDMPs for providers by integrating PDMP data into health information exchanges, increasing the likelihood that prescription history information will be used in clinical decision-making. Furthermore, many EHR systems also integrate electronic prescribing of controlled substances (EPCS). The American Medical Association (AMA) and the American College of Physicians both recommend EPCS as one of the top tactics to combat opioid abuse, as eliminating paper prescriptions will improve accuracy, reduce diversion and fraud, as well as improve data quality to PDMPs. However, only the States of Maine and New York have mandated the use of electronic prescribing for controlled substances (Minnesota has mandated e-prescribing since 2011, but no enforcement mechanism exists), and these states are using Medicaid reimbursement rates to incentivize providers to use EPCS. Other states have followed suit; Virginia passed legislation mandating statewide EPCS to take effect in 2020. More recently, Commission member Governor Cooper signed the Strengthen Opioid Misuse Prevention (STOP) Act which, as of July 1, 2017, requires electronic prescribing of certain schedule II and III controlled substances, including opioid medications, in North Carolina. Practitioner ability to electronically prescribe controlled substances in the United States is currently governed by an interim final rule, which would benefit from a revision so practitioners can take advantage of modern technology that would make registration and use of this service easier.

Practitioners are also hesitant to use PDMPs because they often do not know what to do when they identify patients with a potential SUD. Physicians and other health professionals often do not have adequate training in SUDs to assess patients and may need coaching on how to effectively address the issue of a potential SUD. This is especially relevant if the PDMP indicates a high-risk patient requiring tapering, alternatives for pain management, and specialty treatment for OUD. Inadequate patient support or treatment may compromise the value of the PDMP,[186] and promote a transition to illicit opioids if prescription opioids are eliminated. In addition, providers are typically pressed for time and often complain that if a patient is flagged by a PDMP they are either ill-equipped to screen for an SUD and/or unable to make a successful referral to specialty SUD treatment programs. ASAM strongly recommends that prescribers be trained in engagement strategies that result in linking patients to treatment when indicated. Integrated decision support tools, such as the screening tools used in SBIRT interventions, could also help practitioners make a quick determination about the likelihood of a SUD and to recommend appropriate specialty care or an appropriate specialty treatment provider at which to obtain an assessment.

There are a number of new and innovative tools for providers to determine which patients are at risk of adverse effects from prescription opioids, including accidental overdose or development of an SUD. Some are used at the provider level and some analytic tools are used at the payer level to flag certain patients for follow-up or interventions.

14. **The Commission recommends that PDMP data integration with electronic health records, overdose episodes, and SUD-related decision support tools for providers is necessary to increase effectiveness.**

15. **The Commission recommends ONDCP and DEA increase electronic prescribing to prevent diversion and forgery. The DEA should revise regulations regarding electronic prescribing for controlled substances.**

Organizations such as the Association of State and Territorial Health Officials (ASTHO) and Palantir recommend that multiple data sources should be integrated, accessible, and up-to-date in PDMPs to rapidly predict and detect outbreak "hot spots" and disease clusters for both public health and law enforcement purposes.[187] Medical providers would benefit from knowing if patients overdosed so they can adjust their treatment, but currently those records do not flow back to primary care from emergency rooms or emergency responders because, in many medical settings, the differing EHR systems are not sufficiently interoperable. Patient privacy laws, while well-meaning, can also hinder the ability to share this information between medical providers. However, the Department of Transportation (DOT) maintains a database of EMT responses for overdoses that could inform PDMPs about patients' level of risk and provide better decision-making tools for the prescriber.

16. **The Commission recommends that the Federal Government work with states to remove legal barriers and ensure PDMPs incorporate available overdose/naloxone deployment data, including the Department of Transportation's (DOT) Emergency Medical Technician (EMT) overdose database. It is necessary to have overdose data/naloxone deployment data in the PDMP to allow users of the PDMP to assist patients.**

Prescription Take-Back Programs and Drug Disposal

The National Prescription Drug Take Back Day, organized by the DEA with state and local partners, provides communities a safe and convenient way to dispose of their unneeded prescription drugs, while educating the public about the dangers for the public of abuse and misuse. Providers wrote nearly a quarter of a billion opioid prescriptions in 2013. This is enough for every American adult to have a bottle of prescription opioids.[188] Many misusers of prescription drugs have indicated they received prescriptions from their family and friends' medicine cabinets.[189]

DEA's Take Back Day, which is held twice a year, provides an opportunity for communities to dispose of their unneeded prescriptions. In addition, these events are often community driven and offers the public a venue to host community health fairs and provide information about drug screening and treatment services. Offering drug screening and treatment information and resources during Take Back events encourages friends and family of loved ones with a substance abuse problem to obtain information and support on a convenient walk in basis. There is also a need to leverage resources by collaborating with other health professionals that offer comprehensive health and substance use services.

States have also established year-round take-back programs in partnership with community stakeholders and local law enforcement agencies. North Carolina's 'Operation Medicine Drop' is

the largest take-back program in the U.S., and has collected nearly 89.2 million pills at more than 2000 events since 2010.

There is an opportunity to increase efforts by encouraging hospitals/clinics with onsite pharmacies and retail pharmacies to become authorized collectors. Authorized collectors provide a year-round opportunity for the public to properly dispose of their unused prescriptions. Onsite and retail pharmacies have a tremendous opportunity to aid in increasing collection rates by considering incentivizing the public to drop off their unneeded prescriptions by offering store rebates.

In addition, the Federal Government supported the development of drug deactivation bags to allow the safe disposal of old prescription opioids. Drug deactivation bags would be particularly useful in rural areas where an authorized collector may not be nearby. The use of such bags would complement Take Back Day events and give consumers more options. Furthermore, the Federal Government could explore a potential partnership with onsite and retail pharmacies to fund and include a drug deactivation bag with opioid prescriptions. This would provide an opportune moment at the time of drug dispensing to educate the patient on and encourage safe drug disposal.

17. The Commission recommends community-based stakeholders utilize Take Back Day to inform the public about drug screening and treatment services. The Commission encourages more hospitals/clinics and retail pharmacies to become year-round authorized collectors and explore the use of drug deactivation bags.

Pain Level as an HHS Evaluation Criteria

As a condition of full reimbursement of hospitals, the Centers for Medicare and Medicaid Services (CMS) requires that hospitals randomly survey discharged inpatients using the post-hospitalization survey *the Hospital Consumer Assessment of Healthcare Providers and Systems* (HCAHPS).[190] While hospitals must survey only a small percent of patients and response rates are not high (~18%), some elect to also use email to survey every patient and use these responses to improve their own internal processes. This information is reported as part of the program for hospital ratings, 'Hospital Compare,'[191] which offers a public data tool for prospective patients. The tool allows comparison of hospitals across the US on these and other metrics related to patient outcome. During Affordable Care Act (ACA) implementation, the survey became part of how CMS calculates the VBP Incentive, which gives hospitals maximal reimbursement when they reach certain targets. HHS previously included the pain question response information in calculations of incentive payments, but in 2017, CMS announced they would stop including the questions in the VBP program calculation. HHS's stated reason for removing the pain questions from the VBP calculation was to ensure there would not be any financial incentive or pressure to prescribe.[192] HHS has removed the former pain management questions and replaced them with pain management communication questions instead. Moving forward, they intend to continue to include them in HCAHPS.

However, providers and provider associations have expressed they are being required to treat pain with opioids to maintain high ratings. Recent published research since has shown that those with new opioid prescriptions post-discharge are more likely to report their pain was always well managed suggesting that savvy providers have figured out that opioids are a way to manipulate satisfaction.[193] This study also found a new opioid claim within seven days of discharge was likely

to be associated with an opioid claim 90 days post-discharge in Medicare.[194] Finally, other studies showed ratings of orthopedists performing knee and hip replacement were higher in patients reporting better pain control and orthopedist ratings and sometimes hospital ratings were also affected.[195,196] The research suggests that the current approach to pain treatment in the hospital that meets the highest level of response is iatrogenic for ongoing (90-day post-hospital) opioid use.

18. The Commission recommends that CMS remove pain survey questions entirely on patient satisfaction surveys, so that providers are never incentivized for offering opioids to raise their survey score. ONDCP and HHS should establish a policy to prevent hospital administrators from using patient ratings from CMS surveys improperly.

Reimbursement for Non-Opioid Pain Treatments

A key contributor to the opioid epidemic has been the excess prescribing of opioids for common pain complaints and for postsurgical pain. Although in some conditions, behavioral programs, acupuncture, chiropractic, surgery, as well as FDA-approved multimodal pain strategies have been proven to reduce the use of opioids, while providing effective pain management, current CMS reimbursement policies, as well as health insurance providers and other payers, create barriers to the adoption of these strategies. In the third Commission meeting, the Commission heard from several innovative pain management and pharmaceutical companies about the need for proper reimbursement of non-opioid pain medications to increase uptake among healthcare providers and limit the use of opioids. For example, the current CMS payment policy for "supplies" related to surgical procedures creates unintended incentives for those that prescribe opioid medications to patients for postsurgical pain instead of administering non-opioid pain medications. Under current policies, CMS provides one all-inclusive bundled payment to hospitals for all "surgical supplies," which includes hospital administered drug products intended to manage patients' postsurgical pain. This policy results in the hospitals receiving the same fixed fee from Medicare whether the surgeon administers a non-opioid medication or not. Any costs the hospital incurs for creating and administering a multimodal pain management strategy essentially get deducted from its fixed fee payment. Thus, purchasing and administering a non-opioid medication in the operating room increases the hospital's expenses without a corresponding increase in reimbursement payment. Dispensing and writing a prescription for postsurgical opioids, on the other hand, costs the hospital very little, especially since most opioids are generic. Inadequate reimbursement significantly hampers providers' ability to utilize non-opioid treatment for postsurgical pain.

A broader range of pain management and treatment services – including alternatives to opioids, physical therapy, computerized pain management educational programming, PDMP checking, evidence-based behavioral health treatment, tapering off opioids, and drug testing to confirm adherence – should be adequately reimbursed by payers, including CMS.

19. The Commission recommends CMS review and modify rate-setting policies that discourage the use of non-opioid treatments for pain, such as certain bundled payments that make alternative treatment options cost prohibitive for hospitals and doctors, particularly those options for treating immediate post-surgical pain.

Reducing and Addressing the Availability of Illicit Opioids

Along with reducing the supply of unnecessary prescription opioids, a major component of prevention is reducing the number of illicit opioids available on the streets, such as heroin, illicit fentanyl and fentanyl analogues, or diverted prescription opioids. In the Commission's interim report, the Commission recommended prioritizing funding and manpower to federal law enforcement agencies to develop fentanyl detection sensors, to disseminate them to federal, state, local, and tribal law enforcement agencies, and to support federal legislation to stop synthetic opioids from coming into the country through the U.S. Postal Service (Appendix 3). The Commission believes the recommendations outlined below will further address the availability of and staunch the flow of existing and newly emerging dangerous opioids crossing the border into our country.

Improving Data Collection and Analytics

The opioid crisis is both a national security and homeland security threat that impacts the health of individuals and the safety of communities. To respond effectively to this multi-faceted challenge, stakeholders need to access timely and accurate information that provides a comprehensive view of the drug environment at the federal, state, local, and tribal levels. Unfortunately, data on drug use, treatment, and public safety outcomes are managed in different agencies and are often not integrated in a comprehensive way that facilitates the needs of public safety and public health. There is also variability in the way key indicators are defined, collected, and reported across states making it difficult to monitor and assess regional and national trends. It is imperative that all levels of government develop a set of core public health and public safety indicators that can be standardized, collected, analyzed, and shared to inform local, regional, and national prevention, education, outreach, treatment, and enforcement initiatives.

The Federal Government has made considerable investments in capabilities that facilitate collaboration among federal, state, and local agencies to enhance our Nation's ability to address various threats affecting our communities. For example, the CDC has provided federal grant funding to select states to improve prevention and response efforts by supporting more timely public health data collection, disseminating public health surveillance findings to key stakeholders within states, and sharing data with the CDC to support improved multi-state public health surveillance. On the public safety side, the existing models of public health and public safety information sharing have largely been supported by federal grant programs and technical assistance administered through the DOJ's Bureau of Justice Assistance (BJA), and the CDC. Improved coordination among federal departments and agencies related to grant funding and technical assistance activities will expand models of public health, behavioral health, and public safety information sharing and collaboration at the state and local level.

Likewise, states have leveraged Department of Homeland Security (DHS) preparedness grant funding to effectively implement, in collaboration with federal partners, a decentralized and coordinated information sharing environment to identify, analyze, and share public safety information across all levels of government and first responder disciplines. Significant strides have also been made to enhance the Nation's capacity to collect, share, and analyze public safety information, and disseminate actionable and strategic intelligence to key stakeholders from all levels of government. A critical component of the national response to the 9/11 terrorist attacks was the development of a national-level, decentralized, and coordinated information sharing

environment that prioritizes information security and protects individual privacy, civil rights, and civil liberties. State and major urban area fusion centers, the *High Intensity Drug Trafficking Areas* (HIDTA) Program, and Regional Information Sharing Systems (RISS) Centers are some of the key field-based information sharing, analytic, and investigative entities that leverage this capability to enable interjurisdictional and multidisciplinary information sharing, and facilitate collaboration among federal, state, and local public safety partners to address both local and national threats. It is sensible to evaluate how investments in the national information sharing environment could be used to support public health and public safety information sharing and collaboration at all levels of government.

At the state and local levels, successful frameworks for public health and public safety collaboration are expanding. Several states have developed drug monitoring initiatives (DMIs) and overdose fatality review teams, while New York City has developed the RxStat initiative. These efforts integrate various public safety and public health data sets to include drug overdose deaths, non-fatal overdoses, naloxone administrations, prescriber data, drug arrests, drug seizures, and laboratory results. The analysis of these data enables public safety and public health stakeholders to develop and implement prevention, education, outreach, treatment, and enforcement initiatives that protect public safety and reduce drug use and its consequences. These data can be used to develop coordinated risk-reduction strategies tailored to local communities or specific regions.

20. The Commission recommends a federal effort to strengthen data collection activities enabling real-time surveillance of the opioid crisis at the national, state, local, and tribal levels.

In the United States, medicolegal death investigation (MDI) is conducted via a county-based system of medical examiners and coroners (ME/Cs). There are no national standards for conducting MDI in drug overdose cases; including when to investigate a death, any requisite accreditation of ME/C offices and the certification of their investigators, protocols for which drugs to test for and at what cut-off levels, the possibility of suicide, or how or to whom to report findings. The absence of shared standards and procedures prohibits the accurate and timely identification and prioritization of drug threats and the evaluation of the effectiveness of public health and safety policies implemented to abate them. The DOJ and the National Institute of Standards and Technology are currently leading an effort to standardize the process for forensic investigations. Consistency in the investigation and reporting procedures following fatal and nonfatal drug overdose events will permit improvements to the timeliness and completeness of mortality reporting statistics and is necessary to make better and more efficient use of limited state and federal funds.

21. The Commission recommends the Federal Government work with the states to develop and implement standardized rigorous drug testing procedures, forensic methods, and use of appropriate toxicology instrumentation in the investigation of drug-related deaths. We do not have sufficiently accurate and systematic data from medical examiners around the country to determine overdose deaths, both in their cause and the actual number of deaths.

Estimates of the extent of the opioid epidemic in the United States may be underestimated due to inadequate systems reporting information on the number, location, and degree of opioid

consequences. Surveys of chronic drug users and morbidity information could provide timely and in-depth insights into the opioid crises, but were defunded from the budgets of federal agencies. Current data systems do provide some level of measurement, but miss some important aspects of the opioid epidemic. Restoration of funding for these terminated programs is needed to obtain more detailed information on the opioid epidemic.

The unique aspects of opioid drugs exacerbate the issues of monitoring the misuse problem, unlike other illicit drugs such as marijuana, cocaine, or methamphetamine. Cocaine, for example, has been a drug of consequence for decades, is abused by millions of people in the United States, and has limited variations in composition. Data systems monitoring the extent of the cocaine problem have been standardized and institutionalized. Opioids, on the other hand, consist of many drug varieties, including prescription pain medications, heroin, and most recently, illicitly-manufactured fentanyl. Millions of people misuse prescription pain medications, but only a small fraction of that number abuse heroin. These fewer numbers present a challenge for estimating the prevalence of use by the standard federal survey.

For example, the NSDUH, a federal statistical survey of about 70,000 Americans annually (cited often throughout this report), estimated that 600,000 people used heroin in 2010.[197] A study conducted by the RAND Corporation on illicit drug expenditures in America estimated the number of heroin users in 2010 to be closer to 1.5 million.[198] This dramatic discrepancy has been discussed by the press.[199] Illicitly-produced fentanyl, another rapidly growing component of the opioid epidemic is not even routinely tracked by surveys such as NSDUH or drug seizure data systems.

Two discontinued data systems that would provide enhanced fidelity to measuring the extent of the opioid crisis are the *Arrestee Drug Abuse Monitoring* (ADAM) Program and the *Drug Abuse Warning Network* (DAWN). ADAM was a survey of current local high-risk arrestees in jails accompanied by a urinalysis test. Until its termination by the National Institute of Justice in 2003, over 30 jails in cities throughout the country were sampled and tested. These data would provide timely, geo-specific data on opioid use, supported with a confirmatory lab test. The lab analysis could also be adjusted to test for any new opioids appearing in the U.S. market. DAWN was a tabulation of drug mentions in hospital emergency rooms. SAMHSA funded the DAWN program until 2011. These morbidity data would provide a sentinel system, alerting decision makers of the consequences of opioid use before more serious overdoses would occur.

Existing data collection systems, including the major surveys, like the NSDUH and the *Monitoring the Future* study, need to be maintained and improved, and the data gaps need to be filled and revitalized using such novel approaches such as testing wastewater in highly circumscribed regions (e.g. a few blocks) for estimating drug metabolites. This innovative system has already collected biological specimens from high-risk populations for early indications of the changing drug landscape. Population-level data from toxicology screening can also provide a snapshot of drug use and misuse. Local information is essential to complement national data in informing public health and public safety responses to the opioid epidemic.

The possibility of a behavioral health surveillance system at sentinel sites across the country exists for 12+ sites currently under NIDA funding and additional resources have recently been awarded by CDC to 44 states and the District of Columbia to include better tracking of opioid-related overdoses. There is a need for an integrated system that, across the country, can track prevalence rates, treatment modalities, and comorbidities with other illnesses in real-time. Recognizing that there is variability across the United States, these surveillance or sentinel sites can be established for a multitude of local areas across the country.

22. The Commission recommends reinstituting the *Arrestee Drug Abuse Monitoring* (ADAM) program and the *Drug Abuse Warning Network* (DAWN) to improve data collection and provide resources for other promising surveillance systems.

Disrupting the Illicit Fentanyl Supply

The emergence of illicitly produced fentanyl and fentanyl analogues in the drug market has drastically compounded the illicit opioid problem. Increasingly, fentanyl and fentanyl analogues are combined with inert substances and pressed into pill form to be sold as counterfeit prescription opioid pills. To help deter these features of the illicit drug market, changes to sentencing guidelines are underway in many states and in various stages of maturity.

In Massachusetts, any person who traffics' in fentanyl, "by knowingly or intentionally manufacturing, distributing, dispensing or possessing with intent to manufacture, distribute or dispense or by bringing into the commonwealth a net weight of more than 10 grams of fentanyl" faces punishment of up to 20 years in state prison. The term "fentanyl" includes any derivative of fentanyl and any mixture containing more than 10 grams of fentanyl or a derivative of fentanyl. M.G.L.A. 94C § 32E (c ½).

As of July 2017, West Virginia law specifically criminalizes the unlawful manufacture, delivery, transport into state, or possession of fentanyl. W. Va. Code, § 60A–4–415. A violation is a felony, with the following prison terms: (1) if the net weight of fentanyl involved in the offense is less than one gram, such person shall be imprisoned in a correctional facility not less than two nor more than ten years; (2) if the net weight of fentanyl involved in the offense is one gram or more but less than five grams, such person shall be imprisoned in a correctional facility not less than three nor more than fifteen years; and (3) if the net weight of fentanyl involved in the offense is five grams or more, such person shall be imprisoned in a correctional facility not less than four nor more than twenty years.

New Hampshire law defines the term "fentanyl class drug" with reference to a listing of specific substances. N.H. Rev. Stat. § 318-B:1(XI-a.). These drugs are assigned the same criminal penalties as are heroin or crack cocaine. N.H. Rev. Stat. § 318-B:26.

While states consider laws that aim to reduce the supply of fentanyl, including harsher penalties for smaller quantities, given the potency, it is also important to consider whether users, who buy fentanyl unknowingly, could be unnecessarily punished for distribution. For individuals with OUD who are arrested with fentanyl, other factors beyond quantity should be considered to determine possession for personal use versus distribution.

23. The Commission recommends the enhancement of federal sentencing penalties for the trafficking of fentanyl and fentanyl analogues.

As mentioned above, illicit fentanyl and fentanyl analogues are increasingly being pressed into counterfeit prescription opioid pills, often mimicking the appearance of commonly prescribed opioid pain killers such as OxyContin, by Drug Trafficking Organizations (DTOs) and smuggled into the United States in large quantities. While fentanyl seizures are most typically in a powder, salt, or rock-like form, DEA's El Paso Intelligence Center (EPIC) reports an increase in the number of pills seized. In 2016 an estimated 15,632 domestically seized tablets and capsules were

identified by DEA forensic laboratories as containing some amount of fentanyl or fentanyl analogues with or without other illicit drugs and non-narcotic substances. This represents approximately 16 times the number of fentanyl tablets and capsules analyzed by DEA's laboratories in 2014.[200]

Fentanyl in pill form has enabled the development of a more diverse user population that is skewing younger and perhaps more opioid naïve. Moreover, the prototypical experienced intravenous drug user of previous illicit opioid crises has been joined by those who believe they are buying off-market prescription opioids, but are in fact buying fentanyl pressed into pill form.

Furthermore, the online marketplace and cryptocurrencies have empowered a "democratization of the drug trade," where the hierarchical DTOs the United States has effectively confronted for the past several decades no longer have a monopoly on supplying drugs. Rather, individuals can simply go online to one of many internet drug marketplaces and purchase illicit drugs for their own personal use or for further sale on a limited scale, creating a constellation of "micro-networks" across the country that are difficult to locate and nearly impossible to dismantle. The ability to easily purchase drugs like fentanyl online, which are subsequently shipped in a manner and at volumes that make them hard to detect, demonstrates a new pathway for these potent drugs to enter the domestic supply chain. This change carries enormous implications for the law enforcement and justice communities, and requires a framework of relationships, laws and regulations, and procedures to deal with an environment of drug trafficking and use the nation is just beginning to see.

The growing internet drug market, particularly for fentanyl and fentanyl analogues, is a clearly identified critical vulnerability in interrupting the supply of these drugs into the United States. Since the 2013 closing of the first well-known cryptomarket, Silk-Road 1.0, both the clear and the dark web have further expanded the illicit drug market, allowing individuals to purchase dangerous drugs directly from their manufacturers instead of through established trafficking organizations. Internet sales of fentanyl and other synthetic substances has evolved into a direct to consumer market generating large revenues. A Carnegie Mellon University study estimated that revenues from online illicit drug sales increased from between $15-17 million in 2012 to $150-$180 million in 2015.[201] The recent multi-agency and international effort, led by the DOJ, which resulted in the takedown of the Alphabay marketplace was a monumental step forward in this effort.

The dynamics of synthetic drugs and their availability online has the potential to permanently change the drug market. The Federal Government currently lacks a sustained, coordinated, and well-resourced effort to attack the illicit drug online purchase infrastructure to identify and target the network of actors involved, and limit the amount of fentanyl and fentanyl analogues entering the United States.

24. The Commission recommends that federal law enforcement agencies expressly target Drug Trafficking Organizations and other individuals who produce and sell counterfeit pills, including through the internet.

The importation of tableting machines (pill presses) is regulated by DEA. DEA has recently enhanced importation regulations by replacing paper reporting with an electronic process. However, the active use of pill presses remains unregulated. While DEA currently can inspect a registrant's use of controlled substances in their usable form to verify they are well stored and used

for their stated registered purposes, the DEA currently cannot inspect pill presses to verify that equipment is not being used to produce counterfeit drugs.

25. The Commission recommends that the Administration work with Congress to amend the law to give the DEA the authority to regulate the use of pill presses/tableting machines with requirements for the maintenance of records, inspections for verifying location and stated use, and security provisions.

Interdiction and Detection Challenges

The detection of fentanyl and its analogues shipped directly into the United States via international mail and express consignment presents a unique challenge. U.S. Customs and Border Protection (CBP) is responsible for interdicting and screening inbound international mail before all letters, parcels, and packages are released to the U.S. Postal Service (USPS) for domestic delivery.

The CBP operates within nine major USPS International Mail Facilities (IMF), inspecting international mail and parcels arriving from more than 180 countries. CBP partners with the U.S. Postal Inspection Service (USPIS) at each facility to target, detect, and seize international shipments of illicit narcotics, including fentanyl. International mail processing is primarily manual, requiring CBP officers to sort through large volumes of parcels to identify potential shipments of concern. CBP screens all international mail parcels for radiological threats, x-rays all international mail packages presented by USPS, and physically examines those deemed high-risk.

The USPS processed over 275 million international inbound mailings in FY 2016. Of those items, there were over ten million international express mail items and over four million air and surface parcels. In FY 2016, the USPIS initiated 2,439 cases involving drug trafficking and made 1,850 arrests which resulted in 1,571 convictions. Additionally, inspectors seized illegal assets valued at approximately $23.5 million, to include 89 pounds of heroin, 13,968 Oxycodone tablets, and fentanyl-family synthetic opioids on 36 occasions. In these cases, USPIS utilized intelligence derived from drug seizures, international partnerships, and strong relationships with federal, state, local and tribal law enforcement agencies.

Because of the increased threat of fentanyl, and the interagency focus on disrupting the fentanyl supply chain, CBP undertook a pilot program to train canines to detect fentanyl. Although training canines to detect synthetic drugs is a difficult undertaking, the CBP has already trained and fielded canines and placed them in critical locations in the United States to screen incoming parcels to indicate the presence of fentanyl and other synthetic opioids. Canine screening and detection, complemented by the deliberate targeting of shippers associated with fentanyl trafficking, has the potential to increase the likelihood that those containing illicit opioids are seized and removed from the supply chain.

The incredibly high volume of mail, fentanyl's ability to be shipped in very small quantities, a low number of available automated detection systems, and the relatively small number of trained canines make intercepting fentanyl and fentanyl analogues at IMF's monumentally difficult.

26. The Commission recommends U.S. Customs and Border Protection (CBP) and the U.S. Postal Inspection Service (USPIS) use additional technologies and drug detection canines

to expand efforts to intercept fentanyl (and other synthetic opioids) in envelopes and packages at international mail processing distribution centers.

The sheer volume of international mail and IMF infrastructure make interdiction efforts focused on illicit opioids and other drugs a monumental task. One method to address this issue is the increased use of Advanced Electronic Data (AED). Federal regulation requires express package operators to transmit AED prior to package arrival in the United States. AED consists of electronic data about the particulars of each shipment such as sender/receipt names and addresses, contents and quantity. AED's primary use is for advanced targeting for CBP inspections efforts. With AED, CBP can advance-target incoming shipments for additional examination based upon intelligence, prior violations, and other risk factors.

Over 90% of inbound international mail is sent from USPS's top-volume trading partners. USPS now receives AED on inbound packages from 20 countries, including China. International mail services are not required by International law to transmit parcel information prior to arrival in the United States and many do not have the capability to do so even if required. However, international law requires nations establishing such requirements to ensure they can be met by all nations.

To this end, the Commission recommends support of the Synthetics Trafficking and Overdose Prevention (STOP) Act of 2016 or the STOP ACT of 2016, which amends the Tariff Act of 1930 to make the Postmaster General the importer of record for non-letter class mail imported into the United States. The bill amends the Consolidated Omnibus Budget Reconciliation Act of 1985 to impose a duty of $1 on each item of non-letter class mail imported into the United States. The bill amends the Trade Act of 2002 to direct the Department of the Treasury to require the Postmaster General to provide for AED transmission to CBP of certain information on non-letter class mail imported into the United States.

27. **The Commission recommends Congress and the Federal Government use advanced electronic data on international shipments from high-risk areas to identify international suppliers and their U.S.-based distributors.**

28. **The Commission recommends support of the Synthetics Trafficking and Overdose Prevention (STOP) Act and recommends the Federal Government work with the international community to implement the STOP Act in accordance with international laws and treaties.**

DEA reports that diversion of licit fentanyl, either from theft or fraud, currently accounts for about 2-3% of fentanyl-related overdose deaths. However, as government agencies and international partners achieve success disrupting the illicit fentanyl supply chain, there is high confidence that the licit fentanyl, as well as other prescription opioids, stock and supply chain will experience an increased risk of diversion.

In 2011, Commission member Florida Attorney General Bondi fought for the passage of House Bill 7095 Florida Legislature, which aimed to regulate 'pill mills' by combating prescription drug diversion. Specific features of Florida's legislation included adding new criminal penalties, requiring wholesale distributors to credential customers and report on distribution of controlled substances, as well as funding state Regional Drug Enforcement Strike Forces. Within 18 months of the legislation passage, Florida achieved the largest-by an order of several magnitude-year-on-year recorded drops in prescription drug overdose deaths in the nation.

At any point in the manufacturing, distribution, and prescription process, fentanyl, like other prescription opioids, can be diverted for illicit use. The nation should re-examine its current procedures to track the licit supply chain to prevent the diversion of precursor chemicals, partially processed product, and finished material in manufacturing facilities. Additionally, there are few mechanisms to track fentanyl and prescription opioid diversion once the drug is issued by a medical professional to a patient for consumption. One such method could be a requirement for the recipients and users of legally prescribed fentanyl to provide proof, such as empty transdermal patch envelopes or lollipop sticks to a pharmacist before receiving their refills. Another control initiative could be placing restrictions on dispensing fentanyl through the mail, or requiring that packages containing fentanyl or other opioids must be signed for by the recipient.

The DEA must be able to successfully disrupt the diversion of prescription opioid at any and all points in the supply chain.

29. The Commission recommends a coordinated federal/DEA effort to prevent, monitor and detect the diversion of prescription opioids, including licit fentanyl, for illicit distribution or use.

Protecting First Responders from Harmful Effects Resulting from Exposure to Fentanyl and other Synthetic Opioids

The increased prevalence of fentanyl and other synthetic opioids in the illicit drug market requires law enforcement, fire, rescue, and emergency medical services (EMS) personnel to understand how to protect themselves from exposure to these substances. There have been reports nationwide of law enforcement professionals and EMS professionals experiencing opioid overdoses after unknowingly coming into contact with fentanyl residue. Similarly, crime labs do not always have updated policies and procedures for dealing with potentially deadly substances such as fentanyl.

Currently, fear and misinformation regarding potential health concerns to first responders are hindering response efforts and increasing the risk to first responders. To make the environment more challenging, fentanyl can be present in a variety of forms (e.g., powder, tablets, capsules, solution, etc.).

At the state and federal level, there is no systematic method of tracking and examining reports of first responder opioid intoxication due to inadvertent exposure to fentanyl. Establishing uniform data collection and sharing protocols across states, including conducting confirmatory testing and collecting specific information about each incident of suspected first responder opioid intoxication, would assist the first responder community in validating and refining safety recommendations.

The White House convened and coordinated an interagency working group that included medical, public health, law enforcement, and EMS subject-matter experts to develop a set of scientific, evidence-based recommendations for first responders to protect themselves from the harmful effects associated with fentanyl exposure.

As noted in Appendix 4, the *Fentanyl Safety Recommendations for First Responders* are included in this report to maximize awareness.

The Commission commends the Federal Government for providing unified recommendations to frontline personnel. We also acknowledge the interagency working group for recognizing the value

of incorporating feedback from stakeholder representatives from the medical, public health, occupational safety and health, law enforcement, and fire/EMS fields.

30. The Commission recommends the White House develop a national outreach plan for the *Fentanyl Safety Recommendations for First Responders*. Federal departments and agencies should partner with Governors and state fusion centers to develop and standardize data collection, analytics, and information-sharing related to first responder opioid-intoxication incidents.

Opioid Addiction Treatment, Overdose Reversal, and Recovery

Drug Addiction Treatment Services

In the interim report, the Commission reported that the use of MAT has been associated with reduced overdose deaths, retention of persons in treatment, decreased heroin use, reduced relapse, and prevention of the spread of infectious disease. The Commission recommended several steps to increase the use of and access to all forms of SUD treatment, including MAT for SUDs, including removing the federal Institutes of Mental Diseases (IMD) exclusion within the Medicaid program, establishing a federal incentive to enhance access to MAT, and requiring regulators to take enforcement action against health plans that violate the Mental Health Parity and Addiction Equity Act (MHPAEA) (Appendix 3). The Commission also expressed support for the Overdose Prevention and Patient Safety Act/Protecting Jessica Grubb's Legacy Act, and the need to update patient privacy laws, such as 42 CFR Part 2, to ensure that information about SUDs are made available to medical professionals treating and prescribing medication to patients. Building off the previous recommendations, the Commission supports implementation of the steps outlined below to remove additional barriers and further improve access to and quality of drug addiction treatment services across the nation.

Increase Screenings and Referrals to Treatment through CMS Quality Measures

There is a great need to ensure that health care providers are screening for SUDs and know how to appropriately counsel, or refer, a patient that presents with an SUD.[202] As Commission member Dr. Bertha Madras found in her analysis of a SAMHSA SBIRT program, training practitioners in hospitals and primary care settings in the SBIRT model can be effective in reducing rates of alcohol and illicit drug use. In this 2009 study, nearly 500,000 individuals were screened in six states across health care settings and those that demonstrated alcohol abuse and/or illicit drug use were given a brief intervention, brief treatment, or a referral to specialty treatment.[203] A variety of screening tools were employed, and study sites had differences in population demographics and substance use rates; however, across all sites and demographics, self-reported substance use was less at six months after the initial screen and a brief or more intensive intervention. This research demonstrates the effectiveness of addiction screening in a health care setting, as well as the potential to better utilize primary care medical professionals in areas where there is a shortage of specialty treatment providers.

There are opportunities to further the practice of substance use screenings and referrals through CMS quality measures. CMS has several quality measures throughout their programs (Medicaid, 1115 demonstrations, Innovation Accelerator Program, Medicare, etc.) that could help further the practice of substance use screenings and referrals to treatment. The Federal Government, in coordination with the private sector, has a process through which measures are identified, specified and implemented to assure good patient health outcomes. All federal programs have different purposes and authorities and the selection of measures will vary to reflect those differences. At the same time, federal programs strive to adopt measures that will have strong reach without overwhelming providers with reporting requirements. There are currently several substance use measures being used in federal and private quality assurance programs, and many more under

consideration for adoption. However, measures are not deployed across all programs and, in some cases, do not address some of the gaps in care.

Quality measures for substance use screenings and referrals to treatment should address immediate treatment (24-48 hours) at all points of care for individuals in need of an assessment and treatment for OUD, including hospital induction of MAT, strengthening coordination of care and referral efficacy/improved treatment linkage, follow-up monitoring, and adoption of 'hub-n-spoke' models where specialty providers provide clinical support for primary care-based high need patients. High rates of co-morbidity with mental health disorders also warrant substance use screenings when a mental health diagnosis has been made.

31. The Commission recommends HHS, CMS, the Substance Abuse and Mental Health Services Administration (SAMHSA), the VA, and other federal agencies incorporate quality measures that address addiction screenings and treatment referrals. There is a great need to ensure that health care providers are screening for SUDs and know how to appropriately counsel, or refer a patient. HHS should review the scientific evidence on the latest OUD and SUD treatment options and collaborate with the U.S. Preventive Services Task Force (USPSTF) on provider recommendations.

Evidence-based Improvements to Treatment

Addiction is a chronic relapsing disease of the brain which affects multiple aspects of a person's life. In addition to efforts to improve access to treatment, public policy should also seek to improve the efficacy of treatment. Effective treatment must address the needs of the whole person to be successful. Research by NIDA outlines 13 principles upon which effective treatment programs and practices are built.[204] Grounded in these principles, a growing body of evidence-based models guides the work of addiction treatment.[205] Models demonstrating the greatest outcomes tend to incorporate behavioral, psychosocial, and pharmacological elements, if available,[206] and are tailored to the individual client. The ability to adopt evidence-based models depends on provider ability to support skilled staff who are appropriately credentialed and/or licensed to implement necessary practices. Insurers and other payers can create pressure on treatment providers for a consistent, high-quality standard of care.

Treatment should include the following five elements:[207]

1. Complete evaluation for OUDs by a qualified medical professional including co-occurring other SUDs, psychiatric disorders, and medical disorders.
2. Access to MAT (e.g., methadone, buprenorphine/naloxone, naltrexone). Choice of medication should be made by a qualified professional in consultation with patient, and based on clinical assessment.
3. Simultaneous access to adjunctive psychosocial treatment that may include: group therapy, individual counseling, family therapy, relapse prevention, other psychosocial treatment. These services may be delivered in a variety of levels of care depending on what is clinically appropriate including inpatient, outpatient, intensive outpatient, residential, or partial hospitalization, depending on what is clinically appropriate for the client based on assessment.[208]

4. Treatment of co-occurring psychiatric disorders: The majority of patients with OUDs have co-occurring psychiatric disorders, especially trauma related disorders such as PTSD, depression, and anxiety disorders. Patients with OUDs who do not receive treatment for these mental health conditions generally have poor treatment outcomes.
5. Treatment of co-occurring medical conditions: Patients with OUDs may require treatment for the many medical conditions (e.g., cardiac, infectious, dermatologic, among others).

Connecting treatment to social supports, such as stable housing, employment/job training, education/vocational training, medical care, transportation, child care, etc. is also needed on an ongoing basis to help the individual be successful in their recovery and rebuild a lifestyle that is healthy and productive.[209,210] Reports by the Agency for Healthcare Research and Quality (AHRQ) at HHS endorsed process measures that emphasize treatment completion as key to achieving positive behavioral health outcomes. Similarly, the National Quality Forum, an organization that works to make improvements in healthcare, endorsed the adoption of process measures to count and increase the number of adults in MAT programs who receive at least 180 days of continuous treatment.[211] Subsequently, services that facilitate client retention and engagement to at least 180 continuous treatment days will improve client outcomes.

However, providers, practitioners, and funders often face challenges in translating such principles into practice to help individuals achieve positive long-term outcomes. Improving the quality of treatment programs will require increasing the number of skilled psychiatrists, medical practitioners, counselors, recovery coaches, and improving business practices of providers, which facilitates adoption of evidence-based practices such as MAT.[212] Additionally, persons seeking care need user-friendly information on quality program and selection criteria to identify programs that match their needs. Use of evidence-based assessment tools and processes will help determine the appropriate level of care and configuration of services needed by the individual client. Adoption of ASAM's patient placement criteria should guide referral to the appropriate setting, frequency, and duration of services.

32. The Commission recommends the adoption of process, outcome, and prognostic measures of treatment services as presented by the National Outcome Measurement[213] and the American Society of Addiction Medicine (ASAM).[214] Addiction is a chronic relapsing disease of the brain which affects multiple aspects of a person's life. Providers, practitioners, and funders often face challenges in helping individuals achieve positive long-term outcomes without relapse.

Insurance and Reimbursement Barriers to Accessing MAT

There are currently three FDA-approved medications for the treatment of OUD: methadone (an opioid agonist), buprenorphine (an opioid partial agonist) and naltrexone (an opioid antagonist).[215] MAT for OUD is associated with decreases in opioid use, opioid-related overdose deaths, criminal activity, and infectious disease transmission, while improving social functioning and retention in treatment.[216] Despite this, less than half of privately-funded SUD treatment programs offer MAT and only a third of patients with OUD at these programs receive it.[217] Though rural areas have high rates of OUD, treatment options, including those that utilize MAT, are minimal.[218] Furthermore, physicians that have the necessary training and DEA authorization to prescribe buprenorphine are limited in the number of patients they can treat.

There are commercial insurance barriers to MAT, such as dangerous fail-first protocols and onerous and frequent prior authorization requirements. Fail-first approaches require that a patient try counseling or other psychosocial approaches before being offered more intensive forms of treatment, or MAT. Families, consumers, and treatment providers have consistently identified these and other barriers to obtaining insurance coverage for opioid and other SUDs. These practices are not evidence-based and are not a tenable clinical protocol for individuals with OUDs, as they delay treatment and in doing so, open a window for renewed opioid use and potential death.

Prior authorizations may also serve as a barrier, as they can take a significant amount of time and can disrupt the clinical 'moment' when a patient has finally agreed to try treatment. A 2017 survey of physicians indicated that prior authorization requirements by third party payers were the most commonly reported barrier to prescribing.[219] In 2015, 48 Medicaid programs required prior authorization for buprenorphine.[220] With addiction, the initial goal is to rapidly and immediately engage a person in treatment. Rapid response is necessary to secure treatment before an individual goes into withdrawal and seeks drugs illegally in search of relief.

In addition, CMS policies regarding MAT for Medicare recipients are complex and create barriers for Medicare patients seeking access to MAT. Methadone is covered under Medicare Part D when prescribed for pain, but not when given as part of an OUD treatment program. Some MAT reimbursements are part of a bundled payment for inpatient care, but it has come to the attention of the Commission that bundled payments can be a barrier to providers offering an array of services and medications.

33. The Commission recommends HHS/CMS, the Indian Health Service (IHS), Tricare, the DEA, and the VA remove reimbursement and policy barriers to SUD treatment, including those, such as patient limits, that limit access to any forms of FDA-approved medication-assisted treatment (MAT), counseling, inpatient/residential treatment, and other treatment modalities, particularly fail-first protocols and frequent prior authorizations. All primary care providers employed by the above-mentioned health systems should screen for alcohol and drug use and, directly or through referral, provide treatment within 24 to 48 hours.

Reimbursement rates for SUD treatment services are typically lower than those for other health conditions. Private and public insurers complain that they cannot find enough quality providers for their networks. The provision of SUD treatment, often in the form of counseling and psychosocial services, has a different business and service model than other health conditions. Lack of sufficient reimbursement impedes the ability of professionals and practices to implement high-quality and consistent care, including but not limited to the use of EHRs, the implementation of evidence-based practices, and the routine use of quality metrics. Moreover, the disincentives are so significant that many practitioners no longer take insurance, diminishing access to care even when there appears to be sufficient capacity. Such differential reimbursement strategies exist in the hospital setting as well. Hospital chemical dependency units, for instance, are paid lower rates than inpatient psychiatric facilities.

34. The Commission recommends HHS review and modify rate-setting (including policies that indirectly impact reimbursement) to better cover the true costs of providing SUD treatment, including inpatient psychiatric facility rates and outpatient provider rates.

Enforcing the Mental Health Parity and Addiction Equity Act (MHPAEA)

Spearheaded by Commission member former Congressman Kennedy, MHPAEA aimed to build upon the patient protections enacted by the Mental Health Parity Act (MHPA) passed in 1996, which provided that large group health plans could not impose annual or lifetime dollar limits on mental health benefits that are less favorable than any such limits imposed on medical/surgical benefits. In other words, parity is a simple concept that requires health insurance plans to offer behavioral health coverage that is comparable, and equal to, the coverage for physical health. In reality, creating appropriate parity regulations, and enforcement of parity laws, is far from simple.

MHPAEA extended these parity requirements to SUDs, but legislation did not require large group health plans and health insurance carriers to cover mental health or SUD benefits. The Affordable Care Act changed this by requiring coverage of mental health and SUD services as an essential health benefit in individual and small group plans.

However, while parity is a legal requirement, the existing means of monitoring and enforcing the parity act are insufficient. The sole means of enforcement under the parity act is equitable relief against the buyer of the insurance plan; and for the employer-based plans that are self-funding, DOL is presently permitted to enforce MHPAEA against only the employer, rather than the insurance company administering the benefits. The Commission heard from numerous organizations, such as the Parity Implementation Coalition, the Partnership for Drug-Free Kids, the National Council for Behavioral Health, Shatterproof, ASAM, and the American Academy of Addiction Psychiatry, about the need to systematically monitor and enforce MHPAEA to ensure parity in the coverage of mental health and addiction services.

MHPAEA has been the impetus for much progress towards parity for behavioral health coverage; plans and employers have, by and large, done away with policies that are clear violations; provisions such as dollar-limits, visit limits, and outright prohibitions on certain treatment modalities that exist only on behavioral health benefits. However, what remains are violations that are murkier and harder for regulators to discern, for example, non-quantitative treatment limits (NQTLs). These hurdles include medical necessity reviews that are more stringent on the behavioral health side than the medical/surgical side, limited provider networks, and onerous prior-authorization requirements. In reality, it is often difficult to discern when a behavioral health benefit is “on par” with a medical/surgical benefit as different care settings and diagnoses have different policies regarding benefits, providers, and authorizations.

One goal of MHPAEA and other parity laws was to address cost-shifting from the commercial sector to the public sector for the financing of substance use and mental health treatment. Expanding the private sector share of expenditures could increase access to treatment for opioid and other drug use disorders. As of 2014, private cost-sharing did not increase in proportion to the private sector share of the insurance market. It financed only 18% of SUD treatment in 2014. Legislative changes providing DOL with the ability to impose a civil monetary penalty, such as those provided for violations of the Genetic Information Nondiscrimination Act (GINA), would encourage private insurance companies, and employers, to satisfy their legal obligations under MHPAEA and in turn, ensure they are adequately doing their part to address the country's opioid epidemic.

HHS has built an online portal to help individuals who have trouble accessing behavioral health services, including addiction treatment. This portal, available at https://www.hhs.gov/mental-health-and-addiction-insurance-help/index.html, directs individuals to different sites, including

DOL, depending on the type of insurance coverage. The Commission applauds this project as well as the other activities of the Federal Mental Health and Substance Use Disorder Task Force in working towards public education and full parity compliance.

Building upon the recommendations provided in the interim report, the Commission believes the following actions will help to ensure parity violations do not impede access to substance use treatment.

35. Because the Department of Labor (DOL) regulates health care coverage by many large employers, the Commission recommends that Congress provide DOL increased authority to levy monetary penalties on insurers and funders, and permit DOL to launch investigations of health insurers independently for parity violations.

36. The Commission recommends that federal and state regulators should use a standardized tool that requires health plans to document and disclose their compliance strategies for non-quantitative treatment limitations (NQTL) parity. NQTLs include stringent prior authorization and medical necessity requirements. HHS, in consultation with DOL and Treasury, should review clinical guidelines and standards to support NQTL parity requirements. Private sector insurers, including employers, should review rate-setting strategies and revise rates when necessary to increase their network of addiction treatment professionals.

MAT in the Criminal Justice System

In the weeks following release from jail or prison, individuals with or in recovery from OUD are at elevated risk of overdose and associated fatality. MAT has been found to be correlated with reduced risk of mortality in the weeks following release and in supporting other positive outcomes. A large study of individuals with OUD released from prison found that individuals receiving MAT were 75% less likely to die of any cause and 85% less likely to die of drug poisoning in the first month after release.[221] Compared to approaches that do not include FDA-approved medications, MAT for OUD is associated with better treatment retention,[222] reductions in the spread of infectious diseases, such as HCV and HIV, and lower rates of criminal behavior.[223,224,225,226,227,228]

Despite the research evidence, a national survey of corrections staff in 14 states found very limited use of MAT. While 83% of prisons and jails offered some form of MAT, its use was limited mostly to detoxification or to maintenance treatment for pregnant women.[229,230] One study found that nearly 60% of jail personnel surveyed strongly disagreed with the statement that their tax dollars should support methadone treatment. The same survey found that nearly 55% of jail security personnel agreed with the statement that "people who overdose on heroin get what they deserve." Twelve percent of jail health services staff shared this perspective. The authors noted that negative attitudes regarding MAT appeared to be related to negative judgments about drug users in general and heroin users in particular.[231] While the National Institute on Corrections (NIC), the BJA, the National Association of Drug Court Professionals (NADCP), and other entities have made significant strides in educating correctional administrators and practitioners, much progress remains to be made.

Warranting special concern are pre-trial detainees involved in the criminal justice system. The population of pre-trial detainees is several times larger than the population of individuals sentenced

to jail. These individuals may be less likely to receive treatment and other services due to the fact that they may be released or transferred in a relatively short period of time. Increasing access to treatment, and especially MAT for OUD among these individuals is critically important. Doing so can save lives and reduce future public safety and public health costs associated with unchecked opioid addiction among these individuals.

37. The Commission recommends the National Institute on Corrections (NIC), the Bureau of Justice Assistance (BJA), the Substance Abuse and Mental Health Services Administration (SAMHSA), and other national, state, local, and tribal stakeholders use medication-assisted treatment (MAT) with pre-trial detainees and continuing treatment upon release.

Drug Courts and Diversion Programs

There is evidence that a large majority of individuals who have an SUD do not receive treatment.[232] Drug courts are a proven avenue to treatment for individuals who commit non-violent crimes because of their SUD. Drug courts have traditionally been a more effective response for non-violent, low-level offenders with SUDs, rather than lengthy prison sentences. A systematic review of drug courts in 30 states published by the Campbell Collaboration in 2012 found that a combination of comprehensive services and individualized care is an effective way to treat offenders with serious addictions. However, 44% of U.S. counties in 2014 did not have a drug court for adults.[233] The principal factors limiting drug court expansion are insufficient funding, treatment, and supervision resources, not a lack of judicial interest. The Commission heard from several organizations, including Advocates for Opioid Recovery, the Addiction Policy Forum, and Young People in Recovery, about the need to implement and oversee these problem-solving courts to create true 'recovery ready communities.'

The U.S. Pretrial Diversion Program diverts certain individuals involved in the justice system for a first or second felony offence to a program of supervision and services administered by the U.S. Pretrial or Probation Services. The U.S. Attorney's Office has the discretion to offer this alternative to eligible individuals. Under the program, diversion typically takes place before charging, although it is possible at any time before trial when a pretrial diversion agreement is executed. The period of supervision is up to 18 months. Drug, reentry, or veterans' courts can be a central component of the pretrial diversion process.

As of June 2015, the National Institute of Justice reported that there were 27 Federal District Courts that operated as drug courts as well as six federal veterans' courts. Generally, Federal District Courts adopting the drug court model or similar approaches for diversion and/or reentry support are designated as Federal Reentry Courts. These courts can encompass pre- and post-adjudication diversion as well as post-incarceration reentry/recovery support. Federal reentry courts concurrently engage probation, parole, the Federal Public Defenders, and U.S. Attorneys' Offices. They utilize a blend of treatment and sanction alternatives to address behavior, rehabilitation and community re-integration for non-violent, offenders who are seeking recovery from SUD.

As a rule, Federal Reentry Courts make MAT available to individuals participating in pre- and post-adjudication diversion and post-incarceration reentry programs. Studies have shown that MAT recipients remain engaged in treatment at higher rates, have fewer positive tests for illicit drugs, and reoffend at lower rates than individuals with OUD not receiving MAT. For incarcerated

individuals, these courts typically incorporate an early-discharge program to replace the final year of incarceration with strictly-supervised release into the drug court regimen. Federal Reentry Courts adopting the drug court model incorporate the 'Ten Key Components' of a drug court program in a voluntary contractual program lasting a minimum of 12-18 months. Court program participants returning to the community from incarceration are transferred to traditional parole supervision following graduation. However, they may continue to receive case management services voluntarily through the reentry court.

Jurisdictions that run drug courts continue to innovate and adjust their programs and policies based on experience and in light of the current opioid epidemic. In Buffalo, NY, the court found that some arrestees were suffering fatal overdose between arrest and their formal entry into drug court. Therefore, they established the first Opiate Intervention Court in the country. This court temporarily suspends adjudication of charges in order to get those at high risk of overdose into treatment. The program is relatively new, but the initial results are promising and other jurisdictions should consider adopting a similar strategy.

38. The Commission recommends DOJ broadly establish federal drug courts within the federal district court system in all 93 federal judicial districts. States, local units of government, and Indian tribal governments should apply for drug court grants established by 34 U.S.C. § 10611. Individuals with an SUD who violate probation terms with substance use should be diverted into drug court, rather than prison.

Addiction Services Workforce and Training Needs

By the year 2025, workforce projections estimate that there will be a workforce shortage in the fields of substance abuse and mental health treatment of approximately 250,000 providers across all disciplines. Workforce needs include addiction psychiatrists, physicians specializing in addiction medicine, counselors, recovery coaches, and other behavioral health providers. There are simply too few physicians and other clinicians with the requisite training to meet the demands of the estimated 19.4 million Americans suffering from untreated SUDs. Expanding the workforce to meet treatment demand will require a comprehensive federal, state, local, public and private effort to develop the workforce pipeline.

Opioid-related inpatient stays and ED visits have increased dramatically across the Nation.[234] Fourteen of the 18 states experiencing the highest rate of opioid overdose deaths have experienced an increase in opioid-related hospital admissions, ranging from 21.4% to 54.6%. Moreover, a recent analysis of private insurance data found that most privately insured patients do not receive recommended care following an opioid-related hospitalization.[235]

Hospital programs are emerging across the country to address these surges in overdoses and improve post-discharge outcomes. One method has been the use of peer recovery coaches and other types of community health workers (CHWs), such as health educators, medical assistants, and community health outreach workers. The American Public Health Association defines a CHW as a "frontline public health worker who is a trusted member of and/or has an unusually close understanding of the community served." These workers are increasingly employed in physician offices and other health settings as care extenders. As such, they are uniquely positioned to be trained to provide substance use screening, brief intervention, referral management, and health and

community linkages in primary care and emergency room settings, and to provide outreach and care to substance using homeless populations.

Peer recovery specialists/coaches are in recovery from an SUD. New programs are emerging across the country to use CHWs and recovery coaches in a range of settings, including hospitals, to provide immediate and ongoing support and treatment linkages to individuals who have overdosed from opioids, or support individuals newly in recovery. These programs can address alarming levels of readmissions due to overdose. In addition, recovery workers are supporting law enforcement, fire departments, and other community partners addressing the opioid overdose epidemic. The use of these types of care extenders can help address the workforce shortage, but more of them are needed.

Recovery coaches are often members of a recovery community organization (RCO), which can and do play unique rolls in helping individuals, families and communities respond to drug use, addiction, and their consequences; they are uniquely positioned to facilitate access to treatment, support retention and successful treatment completion, and provide ongoing services and support after treatment. Unfortunately, they exist in far too few communities. While states such as Vermont and Texas have developed and are expanding and enhancing statewide RCO networks, other states have no RCOs at all or only have RCOs in selected communities. RCOs play a critical role in engaging individuals addicted to opioids and other drugs, linking them to treatment and other needed services and supporting them as they pursue their recovery.

Integral in tackling this epidemic is the recognition that diverse communities experience different rates of mental disorders and/or SUDs, as well as challenges to treatment access. For example, in 2016, the rate of illicit drug use in the last 30 days among American Indians and Alaska Natives ages 12 and up was 15.7%, the highest among all racial demography.[236] Research has shown that integrating culturally-based solutions into evidence-based treatment and recovery programs is a best practice and improves treatment outcomes. RCOs are best positioned to develop and implement culturally-specific ways to address the crisis in their communities.

RCOs are innovators and collaborators, working with hospitals, treatment providers, law enforcement, courts, corrections, child welfare systems, and broader communities to reduce drug use, and helping people achieve and sustain recovery. Their flexibility allows them to rapidly adapt to changing circumstances and to identify and fill gaps in systems and services. To maximize the benefit accrued from RCOs, federal efforts should help better integrate RCOs into local and statewide systems, services and sectors, such as Drug-Free Communities, HIDTA, correctional systems, law enforcement, hospitals, primary care, specialty treatment, and child welfare.

DOL has established an apprenticeship program for CHWs and recovery coaches with standard competencies, a curriculum, educational training, and on-the-job learning components, and routinely provides grants to augment the workforce. Through this program, employers provide a stipend for entry-level CHWs to receive on-the-job learning, on-site supervision, and educational training with the intent to secure employment as a credentialed CHW. Once an apprentice completes the CHW certification program, his or her name is registered into a DOL database, issued a certificate of completion, and is considered certified. The Presidential Executive Order Expanding Apprenticeships in America published on June 15, 2017 encourages federal agencies to fund and provide other supports to expand the use of CHWs to provide critically needed services across the country.[237] Health entities such as hospitals and primary care offices can also sponsor training and employment.

39. The Commission recommends the Federal Government partner with appropriate hospital and recovery organizations to expand the use of recovery coaches, especially in hard-hit areas. Insurance companies, federal health systems, and state payers should expand programs for hospital and primary case-based SUD treatment and referral services. Recovery coach programs have been extraordinarily effective in states that have them to help direct patients in crisis to appropriate treatment. Addiction and recovery specialists can also work with patients through technology and telemedicine, to expand their reach to underserved areas.

Estimates suggest there are currently about 4,400 actively practicing certified addiction specialist physicians (addiction medicine and addiction psychiatry) in the country, but data on the specialty workforce is limited. About 8 years ago, an estimate was made of the need for 6,000 addiction specialists, but that number is now insufficient given the growth of the opioid epidemic.

Addiction medicine was only formally recognized as a medical subspecialty in 2016. Currently, 46 of the Nation's 160 accredited medical schools offer addiction medicine fellowships. The first-ever addiction medicine board exam was held in September 2017. By 2021, fellowships will be the only pathway for physicians to take the addiction medicine certification exam. Without an adequate number of fellowships producing at least two new fellows per year, the field will quickly atrophy. Therefore, it is important to quickly ramp up the numbers of fellowships to address the opioid crisis. The goal is to grow the fellowships to 125 over the next five years. Significant funding is needed to start and sustain fellowship programs.

The Health Resources and Services Administration (HRSA) provides unique vehicles for addressing the increasing trends in opioid use, overdose, and addictions across the United States. The agency funds health centers in urban, suburban, and rural areas, trains and strengthens the workforce, hosts the Federal Office of Rural Health Policy, and has grant programs for several high-need and underserved communities and populations. The 21st Century Cures Act included funding for HRSA for addiction medicine fellowships starting in 2018. Starting this year, fellowships will be accredited by the Accreditation Council for Graduate Medical Education, which is a significant step toward getting funding from the VA and others.

Federal agencies should also be considering where telemedicine can play a role in ensuring access to care for those in geographically isolated regions and underserved areas.

40. The Commission recommends the Health Resources and Services Administration (HRSA) prioritize addiction treatment knowledge across all health disciplines. Adequate resources are needed to recruit and increase the number of addiction-trained psychiatrists and other physicians, nurses, psychologists, social workers, physician assistants, and community health workers and facilitate deployment in needed regions and facilities.

41. The Commission recommends that federal agencies revise regulations and reimbursement policies to allow for SUD treatment via telemedicine.

42. The Commission recommends further use of the National Health Service Corp to supply needed health care workers to states and localities with higher than average opioid use and abuse.

Response to Overdose

Expanded Access and Administration of Naloxone

Naloxone is an opioid antagonist medication that can rapidly reverse opioid overdose. It has been available for over forty years, has an excellent safety profile, and can be easily administered by either intravenous or subcutaneous injection or via nasal absorption. In the interim report, the Commission recognized the importance of ensuring naloxone is made as widely available as possible to save lives. Consequently, the Commission recommended that all law enforcement in the United States be equipped with naloxone, model legislation be provided to states to allow naloxone dispensing via standing orders, and 'Good Samaritan' laws be enacted to empower the public to seek help (Appendix 3).

The Commission assessed the availability and accessibility of naloxone across the nation. Figure 5 below shows the means at which the public can access naloxone in community pharmacies widely differs between the states. While there is not necessarily a naloxone supply shortage, price increases of the various forms of naloxone continue to create affordability issues, preventing state and local governments, as well as community organizations, from stocking naloxone at the levels necessary to rescue more people from overdose.

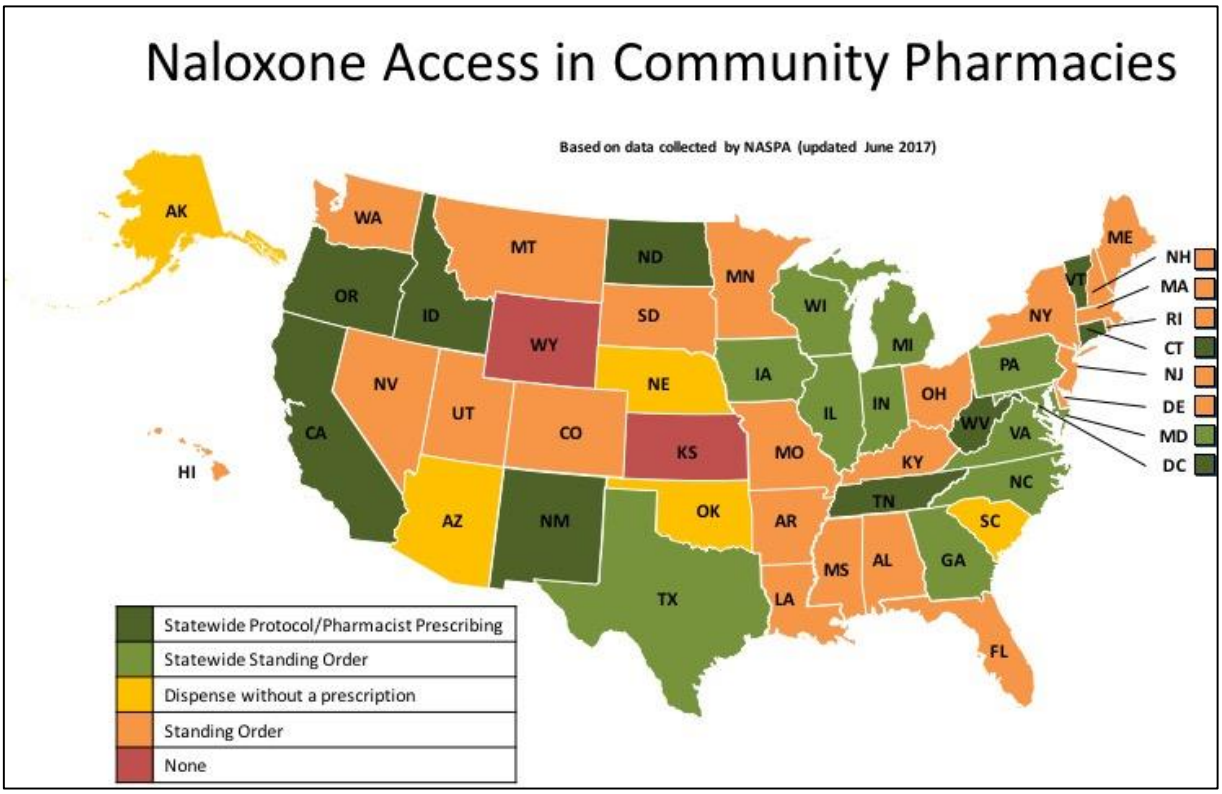

Figure 5. Naloxone Access (Source: National Alliance of State Pharmacy Associations)

To further ensure naloxone is made available when there is the greatest chance of an overdose, we must allow more first responders to be equipped with this life saving drug, including EMS personnel. In 2007, the National Highway Traffic Safety Administration's (NHTSA) issued its

National EMS Scope of Practice Model to provide guidance to states on the minimum skills and knowledge for licensure of each of four levels of EMS personnel; these four levels are:

- Emergency Medical Responder (EMR)
- Emergency Medical Technician (EMT)
- Advanced Emergency Medical Technician
- Paramedic

The *Model* suggests that the first two levels—EMR and EMT—not be approved for the administration of naloxone. Currently several states, following the NHTSA guidelines, prohibit EMRs and EMTs from administering naloxone in cases of opioid overdose. With the onset of the current opioid crisis, this prohibition has become problematic, especially in rural areas where the higher two levels—Advanced Emergency Medical Technician and Paramedic—are less common than in urban or suburban areas. Additionally, even in urban and suburban areas, EMS personnel in the two lower levels may be the first responders to incidents of opioid overdose. Given the critically narrow window that exists in which to administer naloxone to prevent overdose death, there may not be time to await arrival of higher level EMS personnel.

The *Model* has clearly become outdated with regard to its guidance on the ability to administer naloxone by EMS personnel in the two lower licensure levels, especially given the low risk of adverse effects of administering naloxone in either opioid overdose on non-opioid overdose conditions and the development of easily administered, pre-measured dose technologies.

Furthermore, in New Jersey, Commission Chair Governor Christie recently directed his Administration to revise EMS guidelines to allow for higher doses of intranasal naloxone to be administered, as the initial guidelines allowed for 2 mg of naloxone, which proved insufficient for some of the stronger opioids like synthetic fentanyl.

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43. The Commission recommends the National Highway Traffic Safety Administration (NHTSA) review its National Emergency Medical Services (EMS) Scope of Practice Model with respect to naloxone, and disseminate best practices for states that may need statutory or regulatory changes to allow Emergency Medical Technicians (EMT) to administer naloxone, including higher doses to account for the rising number of fentanyl overdoses.

Combination opioid products, especially those co-formulated with naloxone (e.g., oxycodone/naloxone and or buprenorphine/naloxone) have been associated with lower rates of misuse and nonmedical use compared with their single-entity counterparts.[238,239] In the interim report (Appendix 3), the Commission recommended a requirement that naloxone be prescribed in combination with any CDC-defined high-risk opioid being prescribed. Initial studies of the co-prescribing of naloxone with high morphine equivalent narcotic analgesics suggest that co-prescribing can reduce use and abuse of prescription opioids. The results from a 2016 study found a 47% reduction in opioid-related overdoses in the first six months after receipt of the prescription.[240] Initial best practice guidance should be provided based on currently available data and, further, a federally-funded pilot project should be developed to confirm initial findings and clarify the most effective strategies related to co-prescribing.

44. The Commission recommends HHS implement naloxone co-prescribing pilot programs to confirm initial research and identify best practices. ONDCP should, in coordination with HHS, disseminate a summary of existing research on co-prescribing to stakeholders.

Overdose to Treatment and Recovery

Effectively linking individuals who have survived an opioid overdose and those at risk for overdose remains a challenge. However, several promising approaches are emerging. These include, but are not limited to:

- Buprenorphine induction in the ED or other hospital departments followed by linkage with primary care and psychosocial services;
- Methadone induction for hospitalized patients followed by direct linkage to an opioid treatment program (OTP);
- An opioid urgent care unit adjacent to an ED that provides care coordination and linkage to office-based opioid treatment and psychosocial services;
- Overdose prevention training and naloxone distribution in the ED and other hospital settings;
- Post-overdose ED-based engagement, service linkage, and ongoing support and service coordination by recovery coaches and other peer workers who are on-call 24 hours per day, 365 days per year;
- Co-location of recovery coaches and other peer recovery support services workers at opioid treatment programs and primary care practices providing buprenorphine for the treatment of OUD;
- Community outreach and engagement of opioid users, their friends, and family by recovery coaches and other peer workers; and,
- Specialty bedside care for hospitalized patients from an inpatient addiction consult team.

In hospital settings, immediate engagement and initiation of treatment with an FDA-approved medication and/or recovery support services while the patient is still in the ED or is still in an inpatient hospital setting is critically important to increasing the number of Americans with opioid addiction who access treatment, decreasing overdose rates and related fatalities, and gradually lessening the burden the opioid crisis is creating for first responders, hospitals, and communities as a whole. To increase treatment participation, retention, and improve long-term recovery outcomes, a combination of clinical and recovery support services is necessary.

EMTALA requires EDs to stabilize and treat emergency medical conditions regardless of the patient's ability to pay. Medical stabilization language exists in other regulations as well. The general stabilization requirement is to resolve acute symptoms to avoid serious jeopardy to patient health. In the case of an individual with an OUD who has been revived after an overdose, initiation of MAT is often required to stabilize the patient prior to discharge. In addition, appropriate "health extenders," such as CHWs and recovery coaches, are also required to provide treatment engagement and follow-up services. Many emergency rooms and hospitals do not have sufficiently trained staff to diagnose an OUD or to provide the range of MAT and psychosocial services that

are needed to stabilize individuals. Thus, many overdose patients are being released without being appropriately stabilized and are at very high risk for subsequent overdose readmissions.

45. The Commission recommends HHS develop new guidance for Emergency Medical Treatment and Labor Act (EMTALA) compliance with regard to treating and stabilizing SUD patients and provide resources to incentivize hospitals to hire appropriate staff for their emergency rooms.

Recovery Support Services

Over the past decade or more, recovery has re-emerged as a key area of policy, practice, and advocacy. Recovery has many definitions. SAMHSA defines recovery from mental and SUDs as a process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential. Recovery support services (RSS) are non-clinical services designed to help individuals navigate the early stages of recovery and achieve stable, long-term recovery. Several organizations and programs exist to provide a structured and supportive environment for people in long-term recovery and are an emerging infrastructure with approximately 100 national organizations. However, national standards delineating the essential components, as well as financing and operation of state and local RSS, do not exist. The Recovery-Oriented Systems of Care framework identifies relevant values, principles, and strategies. It can be used as a starting point for development of standards.

While national peer RSS organizational accreditation standards have been developed and implemented by the Council on Accreditation of Peer Recovery Support Services, and national peer recovery support services specialist certifications have been developed by the two largest certification bodies in the addictions arena, states have not uniformly adopted these standards. Similarly, while the National Alliance for Recovery Residences has developed recovery housing certification standards that recognize levels of recovery housing, ranging from homes leased and operated by the residents (e.g., Oxford Houses) to residences with linked to clinical services, substandard recovery housing/sober living homes remains a problem in many jurisdictions.

46. The Commission recommends that HHS implement guidelines and reimbursement policies for Recovery Support Services, including peer-to-peer programs, jobs and life skills training, supportive housing, and recovery housing.

Impact on Families and Children

Addiction impacts each member of a family, affecting each member differently, but the most vulnerable are children. Children whose parents have an OUD may be neglected or even require removal to foster care. The developing fetus is vulnerable to substance use by the pregnant mother, as drugs readily cross the placenta and enters fetal blood circulation.

The opioid epidemic has impacted many states with increases in the number of children who have entered foster care due to parental drug use. Child welfare agencies have seen an increase in their

caseloads and are burdened with limited resources, e.g., funds to support drug treatment or parenting classes and community-based support for these children.

Stakeholders in the child welfare arena must collaborate to identify best practices to support families and intervene sooner. Successful treatment for parents can take multiple attempts and requires varied support from many agencies and community-based groups (e.g., treatment providers, counseling, supportive housing, drug courts, parenting classes, and transportation). Once a child enters foster care, the time frame for reunification with their parents or the termination of their parental rights begins. While this varies state by state, due to the scope of the problem it is critical that social workers and child protection staff are equipped to identify substance use early. In New Jersey, Commission Chair Governor Christie announced in September 2017 that the state's Department for Children and Families would be addressing these issues in a multi-prong approach; training Child Protection workers in SUDs, creating a program of peer-support for parents involved with the child welfare system, and increasing the investment in supportive house ("Keeping Families Together" program) for families involved in the child welfare system that experience parental SUD and housing instability.

Children who are in foster care are at greater risk for mental health problems, poor physical health, experience more adverse family experiences and more likely to be suspended from school.[241]

The number of children experiencing NAS increased 383% during the period 2000-2012 (1.2 cases per 1000 hospital births in 2000 to 5.8 cases per hospital births in 2012).[242] To address the number of children born with NAS, the passage of the Comprehensive Addiction and Recovery Act (CARA) of 2017 has modified state requirements related to how states must address SUDs, NAS and Fetal Alcohol Syndrome. Section 503 of CARA recommends that states implement a plan of safe care, yet the requirement does not identify a lead agency to oversee and ensure its implementation which continues to ensure a gap in leadership on this issue.

47. The Commission recommends that HHS, the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Administration on Children, Youth and Families (ACYF) should disseminate best practices for states regarding interventions and strategies to keep families together, when it can be done safely (e.g., using a relative for kinship care). These practices should include utilizing comprehensive family centered approaches and should ensure families have access to drug screening, substance use treatment, and parental support. Further, federal agencies should research promising models for pregnant and post-partum women with SUDs and their newborns, including screenings, treatment interventions, supportive housing, non-pharmacologic interventions for children born with neonatal abstinence syndrome, medication-assisted treatment (MAT) and other recovery supports.

Supporting Collegiate Recovery and Changing the Culture on College Campuses

When American parents send their high school graduates to college, often at huge financial sacrifice, they hope to launch their children in pursuit of their American dream. Unfortunately, too many students get caught up in drug use and binge drinking, putting both their health, academic, extracurricular, and future prospects at risk. Many of these young people are unable to complete their studies. When they do achieve recovery, they are faced with the challenge of returning to the lion's den—a college or university campus where alcohol misuse and drug use may be the norm

for large portions of the student body. It is not surprising that researches have characterized higher education campuses as "abstinence-hostile environments." As more young people find recovery in their teens, they and their parents face the similar challenge of identifying a college or university that will not put their recovery at risk.

In face of this a growing number of colleges and universities have established collegiate recovery programs (CRP). These programs offer support and assistance to students in recovery and to students seeking help for alcohol and other drug problems. To join, some CRP's require treatment completion and/or a specified period of abstinence coupled with mutual aid participation while others are open to any student who believes they have an alcohol or other drug problem or who simply wishes to be part of a community for which alcohol or other drug consumption is not a part of social and recreational activities. Some CRPs provide a dedicated dorm or recovery residence for members and others do not.

Rutgers University, New Jersey's flagship state university system has the longest-running CRP in the nation. The Rutgers CRP began in 1983, with dedicated housing added in 1988. For the student residents, the program provides recovery support, a substance-free living environment, and a variety of extracurricular and enrichment activities such as outings and intramural sports. Students are expected to attend two 12-step meetings each week, and meetings are offered on campus. Rutgers staff regularly provides assistance to colleges and universities around the country who are looking to create or improve programs on their campuses.

To further these programs, New Jersey has passed legislation requiring all state colleges and universities with a significant portion of students living on-campus to have dedicated substance-free housing for students who wish to live in a substance-free environment.

CRPs are relatively small and inexpensive, and provide significant benefits to schools by encouraging degree completion, reducing drop outs, and promoting the health and safety of students. Programs vary, but they commonly include the following components: a coordinator or executive director and small staff; student volunteers; a gathering place, such as a recovery lounge, for students to drop by and support each other and for events; academic advice for those seeking to return to or stay in school; scholarships for those in need who are in recovery and maintain good grades; sponsorship of drug and alcohol free events open to all students on campus; leadership, professional development, and other opportunities to speak out about effective solutions to drug and alcohol problems.

In addition to helping students in recovery flourish and succeed academically, CRPs offer an attractive campus community for students who are not in recovery, but wish to avoid alcohol and other drugs. Through their alcohol- and other drug-free events, including football game tailgates and parties, movies, restaurants, music, and theater outings, they offer safer and healthier alternatives not only for members, but for a range of other students. While the number of collegiate recovery programs has grown significantly over the past decade, it has been estimated that only 3% of higher education institutions in the United States currently have a CRP.[243]

Although most of the costs associated with CRPs should be financed by the colleges themselves, government agencies can take some modest steps to accelerate adoption of these programs, as highlighted below.

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48. The Commission recommends ONDCP, the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Department of Education (DOE) identify successful

college recovery programs, including "sober housing" on college campuses, and provide support and technical assistance to increase the number and capacity of high-quality programs to help students in recovery.

Employment Opportunities for Americans in Recovery

Americans who are in stable recovery from addiction deserve fair consideration for any job for which they are qualified. There are millions of Americans in recovery from all walks of life. Many of these individuals have past misdemeanor or felony drug-related criminal convictions that can impede or prevent them from securing employment for which they are qualified, even after having paid their debt to society and having achieved decades in recovery. When this occurs, it is not only those individuals who pay a price; their families and communities can be deprived of contributions these Americans might otherwise have been able to make. Laws and rules that impede or prevent employment for people in recovery can be counterproductive, making it more difficult to fully rejoin the community and sustain a life in recovery.

In addition to the barriers created by having a past criminal conviction, those in recovery can face long-lasting barriers to employment due to laws that prohibit the hiring of individuals with a past drug conviction in certain settings. For example, Section 1128 of the Social Security Act prohibits any entity receiving funding under federal health programs, such as Medicaid, Medicare, CHIP, TRICARE, or the VA, to employ individuals who have past felony convictions "relating to the unlawful manufacture, distribution, prescription, or dispensing of a controlled substance" (unless that conviction was related to an act that took place before the enactment of the Health Insurance Portability and Accountability Act of 1996) [42 U.S.C. 1320a–7 (4)]. This ban includes individuals with felony convictions related to the sale of illicit drugs outside of the context of a health care facility and covers not only health professionals, but all categories of staff, including custodians, drivers, administrative support staff, building engineers, mailroom personnel, etc.

Known as collateral consequences of conviction, laws of this kind apply restrictions to individuals that continue after they have completed their sentences. These laws can be found at the federal, state, and local levels. Collateral consequences of conviction can serve an important public safety function. However, to the extent that they impede successful recovery or reentry from incarceration without contributing significantly to public safety, they have the potential to actually undermine public safety, public health, and drug control policy goals. Under an award from DOJ, the American Bar Association created a publicly available comprehensive searchable online database cataloguing over 45,000 collateral consequences and civil disabilities and identifying remedies in instances where they are available.[244,245]

Ultimately, private sector employers are well positioned to play a central role in supporting the hiring and ongoing employment of those in recovery, identifying rules and laws that may impede hiring people in recovery, and increasing treatment access for employees with active addiction.

Employment for those with past drug use is a critical part of the solution to this drug crisis. The State of Florida has decoupled felony convictions and eligibility for certain business or occupational licenses with great success, expanding access to the wide arrays of jobs with licensing requirements.

49. The Commission recommends that ONDCP, federal partners, including DOL, large employers, employee assistance programs, and recovery support organizations develop best practices on SUDs and the workplace. Employers need information for addressing employee alcohol and drug use, ensure that employees are able to seek help for SUDs through employee assistance programs or other means, supporting health and wellness, including SUD recovery, for employees, and hiring those in recovery.

50. The Commission recommends that ONDCP work with the DOJ, DOL, the National Alliance for Model State Drug Laws, the National Conference of State Legislatures, and other stakeholders to develop model state legislation/regulation for states to decouple felony convictions and eligibility for business/occupational licenses, where appropriate.

Support Recovery Housing

There is a critical shortage of recovery housing for Americans in or pursuing recovery. Recovery residences (also known as "sober homes" or "recovery homes") are alcohol- and drug-free living environments for individuals seeking the skills and social support to remain free of alcohol or other drugs and live a life of recovery in the community. Generally, recovery residences do not offer treatment, although some are affiliated with, or are arms of treatment provider organizations that offer counseling or other services to residents, onsite or at a nearby location. Recovery residences strongly encourage attendance at 12-step groups or other mutual aid groups (e.g., SMART Recovery, Women for Sobriety, Celebrate Recovery, etc.) and are generally self-funded through resident fees, or in the case of Oxford Houses or other resident-run homes, shared rent, utility, and food payments. Benefits associated with staying in a recovery residence include decreases in alcohol and drug use, psychiatric symptoms, and arrests as well as increases in employment.[246]

Recovery residences can play a critical role for individuals in outpatient treatment, those exiting residential treatment, homeless individuals in early recovery, those involved in drug courts, those returning to the community from incarceration, and those who may not require residential treatment if they have a living environment that is supportive of recovery, outpatient treatment and/or mutual aid groups. Many who cannot return to a home where there is active drug use or a community where they used drugs find a safe haven in a recovery residence. Importantly, like peer RSS generally, recovery residences can help maximize the public and private investments in treatment by ensuring better long-term outcomes, by sometimes making a lower, less costly level of care possible and, in some instances, by making treatment unnecessary.

Unfortunately, unethical operators have cast suspicion on recovery residences generally and have complicated the efforts of families, treatment centers, and court systems to identify safe, supportive, well run, and affordable recovery housing. Quality recovery residences operate in accordance with accepted national guidelines, such as the standards developed by the National Alliance for Recovery Residents (NARR) or the charter Oxford Houses must follow. Residences that do not meet these or state-established standards can place those they serve at risk. While some states have defined recovery residence licensing criteria and or required their treatment providers to only refer patients to certified recovery residences and Oxford Homes, many have no mechanism for ensuring quality and accountability.

51. The Commission recommends that ONDCP, federal agencies, the National Alliance for Recovery Residents (NARR), the National Association of State Alcohol and Drug Abuse

Directors (NASADAD), and housing stakeholders should work collaboratively to develop quality standards and best practices for recovery residences, including model state and local policies. These partners should identify barriers (such as zoning restrictions and discrimination against MAT patients) and develop strategies to address these issues.

Research & Development

For too long addiction and pain research have been conducted and led by separate research communities and suffered from silos and in some cases excessive pressure from industry at the cost of patient health. The *National Drug Control Strategy* has never included a pain management emphasis despite the fact that prescription opioid misuse still is responsible for most opioid misuse in this country and providing better pain management is essential to preventing prescription opioid misuse and diversion that starts so many people down the path to heroin use. Several federal agencies are best suited for shepherding research initiatives and opportunities to combat the epidemic[247] and enhance treatment options, including alternative pain management strategies, and treatment for vulnerable populations such as pregnant women, and substance-exposed infants. Addressing the gaps with basic, applied research, and development can conceivably expand the range of alternatives to imperfect medications currently used to mitigate pain or treat addiction.

52. The Commission recommends federal agencies, including HHS (National Institutes of Health, CDC, CMS, FDA, and the Substance Abuse and Mental Health Services Administration), DOJ, the Department of Defense (DOD), the VA, and ONDCP, should engage in a comprehensive review of existing research programs and establish goals for pain management and addiction research (both prevention and treatment).

New Pain, Overdose, and MAT Medications

The bounties of scientific research are essential to mitigate the opioid crisis, drug addiction and associated morbidity and mortality. The most practical basic research goals for the current epidemic[248] are to develop: (1) effective analgesics with limited or no abuse liability, i.e. alternatives to opioids; (2) drugs to reverse overdose capable of surmounting newly emerging fentanyl analogs or new psychoactive opioids; and (3) medications that do not engender abuse liability or physical dependence to assist in treating opioid addiction. Each of these areas requires short-, intermediate-, and long-term research strategies. The research goals have been charted and led by the NIDA Director, with support and coordination among the NIH institutes and the NIH Director. NIH has also recruited pharmaceutical companies to develop public-private partnerships in pursuit of these goals. This initiative offers great promise to improve the range of choices for pain management, medications assistance, and overdose reversal. As an example, a NIDA partnership with a pharmaceutical company successfully developed a user-friendly intranasal naloxone formulation that results in blood naloxone levels equivalent to those reached with injection. The FDA approved it in 2015.

Alternatives to Opioid Pain Medications. μ-opioid signaling is among the most effective system to dampen or block pain. The same system also produces pleasurable sensations, even euphoria which drives addictive behaviors. For over a century, medicinal chemists have pursued safer opioids to disconnect pain relief from pleasurable sensations. Opioid over-prescribing in part reflects the limited number of effective medications to treat moderate to severe pain and the compelling need for alternatives. Among the candidate solutions are development of abuse-deterrent formulations, new opioids that trigger "biased" μ-signaling pathways, or target other opioid receptors subtypes, or drugs that modify other receptors, and ion channels involved in

processing or modifying pain sensations, including transient receptor potential vanilloid (TRPV) channels, non-psychoactive cannabinoids, inflammatory pathways, or other modifiers of signaling pathways.

Novel therapeutics are also likely to emerge from a better understanding of pain biology, enabled in part by transformative technologies such as the ability to solve the three-dimensional crystal structure of target proteins or assess pharmacology by computer simulations. Adoption of other transformative technologies, including induced stem cells and CRISPR, can result in more efficient validation of novel compounds through the development of models with better translational fidelity. Clinical studies can also be improved by patient selection and stratification.[249]

Overdose Reversal Interventions. Over 140 Americans die daily from opioid overdoses. The primary reason is that overactivated μ-opioid receptors in brainstem neurons stop natural breathing. Naloxone targets the μ-opioid receptor, but unlike oxycodone, heroin, or fentanyl, instead of activating it, it prevents it from functioning and reverses and overdose, if administered in sufficient time. It has saved thousands of lives, but is ineffective if the person overdosing is alone during a narrow window of time, or if requiring multiple doses to surmount a highly potent opioid.[250] This new challenge is reflected in the rapid rise in overdose fatalities driven by the highly potent drug fentanyl, or even more potent fentanyl analogs. Private partnerships are engaging with NIH to develop higher affinity longer-acting formulations of antagonists, including naloxone, to counteract the very-high-potency synthetic opioids that are now claiming thousands of lives.

Treatments for Opioid Addiction. Research and development are needed to improve the range of medications to assist in treating OUD. Currently, three medications are approved for treating OUD: methadone, buprenorphine, and ER naltrexone. Along with psychosocial support, they comprise the current standard of care for reducing illicit opioid use, relapse risk, and overdoses, while improving social function.[251] Each of these medications has important strengths, but some shortcomings. Methadone is full agonist at the μ-opioid receptor, while buprenorphine is a partial agonist. Both methadone and buprenorphine can be reinforcing and thereby diverted, unlike naltrexone which, like naloxone, blocks the receptor. Compliance with treatment is higher with methadone than with buprenorphine or naltrexone,[252] but overall success in abstinence is imperfect.[253] There is a clear need to develop new treatment strategies for OUDs, including new pharmacologic approaches that focus on modulating activity of the reward circuit through other targets (e.g. neurokinin-1 receptor antagonists or κ-opioid receptors antagonists). Other target receptors and vaccines to prevent brain entry of opioids are under investigation.

Over a longer time-frame, prevention and treatment of opioid addiction will require more exquisite knowledge of the mechanisms underlying pain, reward, loss of control, and how biological and social factors shape the attractiveness of opioids. Treating chronic pain while avoiding misuse is problematic for patients with a prior history of SUD, and more research conceivably will reveal the degree of risk for OUD when people with serious pain are undertreated. Other research voids include brain research imaging of people who overdose one or more times. Recent reports have documented cases of amnesia after an overdose. The extent to which opioids cause significant and possibly irreversible brain damage warrants investigation.

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53. The Commission recommends Congress and the Federal Government provide additional resources to the National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), and National Institute on Alcohol Abuse and Alcoholism (NIAAA) to fund the research areas cited above. NIDA should continue research in

concert with the pharmaceutical industry to develop and test innovative medications for SUDs and OUDs, including long-acting injectables, more potent opioid antagonists to reverse overdose, drugs used for detoxification, and opioid vaccines.

Medical Technology Devices

Research and development in new technologies/devices to assist in the opioid crisis are emerging. Their development should be encouraged. A few examples are offered, with a caveat that few have received FDA approval, while others are in various stages of research and development and have yet to undergo FDA scrutiny or even be sufficiently developed for clinical trials.

- Detection of real-time substance use is a critical step for optimizing behavioral interventions and feedback to prevent drug abuse. Traditional methods based on self-reporting or rapid result urine screening are inefficient or intrusive for drug use detection, and inappropriate for timely interventions. Methods for real-time substance use detection are severely underdeveloped. A new real-time drug use event detection method is being developed that uses data obtained from wearable biosensor. Biosensors are designed to detect and establish thresholds of parameters in a real-time drug use event and to produce wearable biosensor data streams.[254]
- Wearable devices that sense respiratory depression (rings, ear pieces) that can alert the user, a family member, or wirelessly report to a first responder to intervene, or automatically inject naloxone when blood oxygenation levels become dangerously low.
- Apps on electronic devices (phones, watches) that can function as behavioral coaches and reminders.
- Technology devices that transmit findings from smartphones directly into the medical record.
- In home monitoring of vital signs with transmission capability
- Transcranial magnetic stimulation (TMS) for treatment of pain.
- Monitoring appropriate consumption/compliance with medications that contain a transmitter to relay a signal as soon as a drug enters the digestive system. A similar transmitter can be adapted for naloxone use.
- Behavioral monitoring feedback apps that can be as, or more effective than face-to-face behavioral training for addiction.
- Pain reduction devices such as subcutaneous field stimulators, dorsal column stimulators, dorsal root ganglion stimulators, multifidus muscle stimulators, implantable infusion pumps, and sensory cortex stimulators.
- Detection of drug consumption use (drugs/metabolites) in neighborhoods using a waste water collection system positioned in drains within small regions (two block radius) to identify hot zones of distribution and/or use.

54. The Commission recommends further research of Technology-Assisted Monitoring and Treatment for high-risk patients and SUD patients. CMS, FDA, and the United States Preventative Services Task Force (USPSTF) should implement a fast-track review

process for any new evidence-based technology supporting SUD prevention and treatments.

55. The Commission recommends that commercial insurers and CMS fast-track creation of Healthcare Common Procedure Coding System (HCPCS) codes for FDA-approved technology-based treatments, digital interventions, and biomarker-based interventions. NIH should develop a means to evaluate behavior modification apps for effectiveness.

FDA Post-Market Research and Surveillance Programs

The FDA is a key federal agency designed to safeguard public health and safety, including opioids. Of all the drugs approved by the FDA, opioids are causing more illnesses and deaths than any other drug class currently on the market. FDA's timeline of regulatory oversight of opioids from 1911-onward shows a rapid expansion of approval of opioids starting in the mid-1990's and continuing to this day. In 2001, as concerns of addiction and overdoses emerged, the FDA took steps to develop public education regarding prescription drug abuse, packet inserts for patient education, and stronger warnings. Other discrete steps taken to rein in their adverse consequences proved equally ineffective.[255]

In 2016, the FDA once again initiated assessment and implementation of its policies to constrict unfettered prescribing practices. These policies included expanded use of advisory committees, development of warnings and safety information for IR opioid labeling, strengthening post-marketing requirements, updating the Risk Evaluation and Mitigation Strategy (REMS) Program that requires sponsors to fund continuing medical education to providers, at low or no cost, on appropriate use of opioids, expanding access to abuse-deterrent formulations to discourage abuse, and reassessing the risk-benefit approval framework for opioid use.[256] In 2017, the FDA brought IR opioids under its REMS program authorities, along with ER long-acting opioids; however, prescriber education in this program is currently optional for prescribers. Currently, more than 20 opioid analgesic formulations are approved by the FDA and an additional 52 applications for approval are being considered.[257]

The evidence base to guide the use of opioid medications, particularly in the setting of long-term use, is substantially lacking. Over decades, opioids were approved by the FDA with two significant gaps in vigilance: lack of concern of misuse, tampering, and diversion from a legitimate prescription and inadequate post-market surveillance of efficacy for long-term use, addiction, and other long-term consequences (e.g. depression or transition to heroin). The FDA is strengthening the requirements for drug companies to generate post-market data on the long-term impact of using ER/long-acting opioids and accumulate better evidence on the serious risks of misuse and abuse associated with long-term use of opioids, predictors of opioid addiction, and other important issues.

56. The Commission recommends that the FDA establish guidelines for post-market surveillance related to diversion, addiction, and other adverse consequences of controlled substances.

Conclusion

The origins of the current opioid crisis can be traced to a sequence of at least twelve converging events and movements that catalyzed the most devastating drug epidemic in our nation's history. A five-sentence letter to a biomedical journal in 1980, followed by other low-quality articles claiming that opioid narcotics are safe to use universally for chronic pain, bolstered advocacy by pain patients and professional societies to treat pain with opioids. It also instigated the opioid pharmaceutical industry to embrace and exploit the flawed claims with aggressive marketing and "educational outreach." Government agencies and accreditation organizations then designated pain as a fifth vital sign. Without a counterbalancing force appearing in the medical community to question the evidence or conclusions, pain assessment became a preoccupation of healthcare practices and opioid prescribing became an accepted solution.

Prescriptions for opioids surged, now fueled by financial and performance pressures on physicians to satisfy patients using opioids, insurers' unrestrained reimbursements for opioids, an insufficient response of federal regulators, and lack of public unawareness of the hazards of this class of drugs. Poor medical education on pain management, on opioid prescribing, and on screening for high risk patients undermined the ability of conscientious physicians to safely treat pain or addiction.

A nation awash with prescription opioids became fertile ground for diversion by acquisition from medicine cabinets, through rogue pharmacies, rogue physicians, and for opportunistic sellers of illicit heroin, fentanyl, and other deadly opioids. The Commission has reflected on this history, for it is a compelling source for solutions to contain this national nightmare, solutions that are complex and multi-dimensional.

By the very nature of our federal-state-local governance, most solutions require responses at all levels of government. Some need the cooperation and the support of private institutions, such as commercial insurers, companies engaged in data analytics, academic institutions, or individuals who have inadvertently contributed to this crisis. Unintentional contributors to the crisis are recognizing earlier missteps and devising strategies to 'reverse engineer' decisions with prudence.

The goals of the recommendations included in this report are to promote prevention of all drug use with effective education campaigns and restrictions in supply of illicit and misused drugs. To achieve supply reduction, we recommend shaping prescribing practices by improved medical education, by alternatives to pain management, as appropriate, by enhancing physician awareness of high risk patients though substance use, mental, and medical screenings and interrogation of PDMPs, insurance company oversight, and by interdiction of deadly opioids. Treatment and overdose rescue are both distinct and inextricably linked efforts. Overdose rescue procedures need to be opportunistic and include access to trained personnel, to medications, and to treatment services. Administering naloxone to a person who has overdosed and then abandoning them without offering medication and same-day entry to treatment is short-sighted and inadequate.

Treatment services need to be improved, foremost by developing thoughtful national evidence-based standards of care, record-keeping, and long-term support. In view of the need, expansion of services is imperative and so are surmounting barriers – to medications, limited healthcare workforce, to insurance reimbursement – and ensuring high-quality care and long-term recovery support services.

The Commission strongly supports research and development of alternatives to opioids for pain management, treatment and rescue, and of modern medical devices essential to improving our

responses. The Commission also strongly recommends real-time data analytics to inform our mission and accomplishments. Above all, each recommendation should have accountability built-in and be subjected to measurable goals, quantitative solutions, and measurable outcomes. The Federal Government now must develop a level of accountability that has not been imposed rigorously in the past.

Lessons learned. A catalog of lessons learned can guide our nation in devising current solutions and alerting future generations on how to avoid inevitable emerging and potentially devastating drug-related crises. Important lessons can be extracted from earlier imprudence. The current focus on opioids is driven by the devastatingly high death rates. While death is the ultimate catastrophe, many psychoactive drugs with abuse potential do not precipitate an overdose crisis nor death as dramatically as do opioids. Nonetheless, other drugs can be markedly detrimental to the brain, body, and behavior.

- Low quality evidence that opioids are innocuous for chronic pain management was accepted without scrutiny, by the healthcare system, by physicians, medical schools, regulatory bodies, and insurers. High-quality assessment of the addictive potential of orally bioavailable opioids should have been imposed by the FDA.
- Constant vigilance is necessary to recognize if marketing efforts are suppressing scientific evidence (e.g. addiction) and common sense. Early scientific scrutiny of dubious claims should be a key priority of regulatory agencies and physicians.
- Engage all stakeholders when creating standards and actionable outcomes. Do not restrict input to those who passionately favor a substance. Advocates may be less willing or able to see unintended consequences than others.
- The approval process of medications with abuse liability should not be restricted to drug safety and efficacy in short term clinical trials. The drug approval process should expand its oversight and consider the number of doses and duration of a prescription for specific indications, the possibility of misuse, diversion, and tampering, and other consequences not traditionally a component of evidence required in the approval process.
- Anticipate unintended consequences and devise effective data analytics, monitoring, and responses at the outset of a trend. A small, but significant portion of patients and other users or misusers of diverted prescription opioids transitioned to heroin. Screening for OUD when reducing opioid supply or creating a tamper-resistance formulation, and implementing procedures to assist treating OUD patients conceivably could have avoided the transition for some people.
- Apply the lessons learned to current movements to medicalize and legalize other Schedule 1 drugs. The catalyst of the opioid crisis was a denial of its addictive potential.
- Pharmaceutical sponsorship of medical society events needs rigorous oversight and review.
- Without adequate training in pain management and in addiction diagnosis and treatment, the medical establishment was caught off guard and unprepared for iatrogenic opioid addiction. Training in these disciplines should be mainstreamed into every level of medical education, to address the current crisis and to prepare for inevitable iterations.
- Healthcare insurers have a significant role in attenuating this public health crisis. They can reduce opioid supply by declining reimbursement for unnecessary opioid prescriptions, and

facilitate recovery by seamless reimbursement for medications and treatment services. Federal oversight on insurance company practices was inadequate as the crisis expanded.

Current Federal Programs and Funding Landscape

Overview

Congress has not enacted full year appropriations for fiscal year (FY) 2018, which began October 1, 2017. The Federal Government is operating under a Continuing Resolution (CR) that will expire in December 2017. The funding levels presented in this report are consistent with the funding levels represented in the FY 2018 President's Budget, including FY 2018 Request levels and FY 2017 CR (annualized) estimates.

The President's FY 2018 Budget Request supports $27.8 billion for drug control efforts spanning prevention, treatment, interdiction, international operations, and law enforcement across 14 Executive Branch departments, the Federal Judiciary, and the District of Columbia. This represents an increase of $279.7 million (1.0%) over the annualized CR level in FY 2017 of $27.5 billion.

Within this total, the Budget supports $1.3 billion in investments authorized by the *Comprehensive Addiction and Recovery Act* (CARA), the *21st Century Cures Act*, and other opioid-specific programs to help address the opioid epidemic.

FY 2018 Funding Specific to America's Opioid Crisis

Reducing Overdoses. Reducing opioid overdoses, to include identifying those at risk of overdose, the signs of overdose, and expanding the use of naloxone, are key pieces of the Administration's strategy to address the opioid overdose epidemic.

The FY 2018 Budget request for SAMHSA includes $12.0 million for *Grants to Prevent Prescription Drug/Opioid Overdose Related Deaths*. This program will provide continuation grants to 10 states to significantly reduce the number of opioid overdose-related deaths by helping states purchase naloxone, equipping first responders in high-risk communities, supporting education on the use of naloxone and other overdose death prevention strategies (including covering expenses incurred from dissemination efforts), and providing the necessary materials to assemble overdose kits. This program was appropriated $12 million in FY 2016 and $12 million in the FY 2017 CR.

The FY 2018 Budget request for the CDC includes $70.0 million for the *Prescription Drug Overdose Prevention for States* program to cover overdoses from opioids and other drugs, the same level as the FY 2017 CR. This program, which advances and evaluates comprehensive state-level interventions for preventing prescription drug overuse, misuse, abuse, and overdose, is expanding to all 50 states and the District of Columbia in FY 2017. Funds in FY 2018 will support state efforts as well as rigorous monitoring, evaluation, and improvements in data quality at the national level. Funds will also be used to increase uptake among providers of the CDC's *Guideline for Prescribing Opioids for Chronic Pain*, as well as implementation of a coordinated care plan that addresses both opioid and heroin overdose prevention by improving care for high-risk opioid patients.

The FY 2018 Budget request also includes $5.6 million in funding for the CDC to address the rising rate of heroin-related overdose deaths by working to collect near real-time ED data and

higher quality and timely mortality data by rapidly integrating death certificate and toxicology information. This is a small increase above the FY 2016 appropriation and level with the FY 2017 CR. Apart from these programs, the FY 2018 budget request continues to provide funding for expansion of electronic death reporting to provide faster, better quality data on deaths of public health importance, including prescription drug overdose deaths.

Enhancing Prescription Drug Monitoring Programs. PDMPs are an important state-based health care tool. They provide information to health care providers so they can better understand what is being prescribed and intervene before a prescription drug abuse disorder becomes chronic. Currently, PDMPs exist in 49 states.

The FY 2018 request for DOJ's PDMP activities includes $12.0 million for state grants to enhance the capacity of regulatory and law enforcement agencies to collect and analyze controlled substance prescription data. The FY 17 CR level for PDMP activities was $13.0 million, level with the FY 2016 final budget. The purpose of DOJ's PDMP effort is to enhance the capacity of regulatory and law enforcement agencies to collect and analyze controlled substance prescription data. In coordination with HHS, the program aims to assist states that want to establish or enhance a PDMP. Objectives of the program include building a data collection and analysis system at the state level, enhancing existing programs' ability to analyze and use collected data, facilitating the exchange of collected prescription data between states, and assessing the efficiency and effectiveness of the programs funded under this initiative.

The FY 2018 Budget for SAMHSA includes $58.4 million for the *Strategic Prevention Framework*. Within this amount, SAMHSA will target $10 million to address prescription drug (including opioids) abuse and misuse, use PDMP data for prevention planning, and implement evidence-based practices and/or environmental strategies aimed at reducing prescription drug abuse and misuse. The final spending level for the *Strategic Prevention Framework* program was appropriated $119.5 million in FY 2016; in FY 2017, the CR level was $119.3 million.

Medication-Assisted Treatment Programs. MAT is an evidence-based treatment for individuals with OUDs. However, it is underutilized and often not available to those who could benefit from its administration. Expanding access to MAT, in combination with other behavioral health care, will help address this issue and help more individuals sustain their recovery from OUDs.

The FY 2018 Budget includes $25.0 million for SAMHSA, to support the *MAT for Prescription Drug and Opioid Addiction* program for states, level with funding for FY 2016 and the FY 2017 CR. In FY 2018, SAMHSA plans to expand and enhance its program to improve access to MAT services for treating OUDs. SAMHSA anticipates 22 new states that have demonstrated a dramatic increase in treatment admissions for OUDs will be funded under the FY 2018 request.

Medication-Assisted Treatment in the Criminal Justice System. The Bureau of Prisons' (BOP) budget contains $1.0 million in new resources to expand the MAT Pilot. The pilot provides an opportunity to evaluate whether MAT should be expanded in the corrections setting.

Residential Substance Abuse Treatment. The Office of Justice Program's budget contains $12.0 million for the Residential Substance Abuse Treatment (RSAT) program for state prisoners, level with funding for FY 2016 and the FY 2017 CR. The program was established to help state and local governments develop, implement, and improve residential substance abuse treatment

programs in correctional facilities, and establish and maintain community-based aftercare services for probationers and parolees. It is intended improve public safety and reduce criminal recidivism by helping offenders become drug-free and learn the skills needed to sustain themselves upon return to the community.

Enhanced Drug Enforcement Efforts. The Budget provides increases to federal law enforcement agencies aimed at reducing the flow of illicit drugs into the country and increasing investigations of transnational criminal organizations, violent gangs, and drug traffickers. Specifically:

The FY 2018 Budget includes funding to maintain and expand capacity to fight against heroin and other illicit drugs at the DOJ. This includes a total of $2.6 billion for the DEA, including $21 million in new discretionary resources are requested for DEA and $32 million in new mandatory resources for the DEA's Diversion Control Program to reduce the diversion and abuse of pharmaceutical controlled substances and listed chemicals, including prescription opioids. The overall DEA request for FY 2018 is an increase of $158.1 million over the FY 2016 level and $150.3 million over the FY 2017 CR level. The FY 2018 Request for the DOJ also includes $526.0 million for Organized Crime and Drug Enforcement Task Force (OCDETF) to support heroin enforcement efforts, address transnational organized crime, and to reduce violent crime in cities across the nation. The request is an increase of $14.0 million above the FY 2016 and $15.0 million more than the FY 2017 CR and will enhance heroin enforcement efforts, address transnational organized crime, and reduce violent crime in cities across the nation.

Drug Prevention. The *Drug Free Communities (DFC) Support Program* is built upon the idea that local problems require local solutions. DFC funding provides for the bolstering of community infrastructure to support environmental prevention strategies to be planned, implemented, and evaluated in communities across the United States, Territories and Protectorates. The DFC Program is guided by local communities who identify and develop evidence-based strategies to reduce drug use and its consequences. For FY 2018, $91.8 million will fund approximately 659 DFC grants and continue the DFC National Cross-Site Evaluation. This program received $95.0 million in FY 16 and $94.8 million in FY 2017 through CR.

Addressing Domestic and Transnational Organized Crime. The Administration will employ tools to disrupt the flow of illicit drugs into our country, and reduce drug trafficking domestically.

In an effort to enhance security at the Southwest Border, in the FY 2018 President's Budget, CBP requests $260.5 million to fund acquisition, delivery, and sustainment of prioritized border security capabilities. This is a new activity, reflecting the President's commitment to border security.

The *HIDTA* program, created by Congress with the Anti-Drug Abuse Act of 1988, aids federal, state, local, and tribal law enforcement agencies operating in areas determined to be critical drug-trafficking regions of the United States. A total of $246.5 million is requested for the HIDTA program in FY 2018, a decrease from the FY 2016 funding level of $250.0 million and the FY 2017 CR funding level of $249.5 million.

The Comprehensive Addiction and Recovery Act (CARA)

The *Comprehensive Addiction and Recovery Act* (CARA) authorized new programs to help fight the scourge of opioid abuse plaguing our Nation, and authorized appropriations for existing programs to continue their work. Highlights of these programs are below:

In FY 2018, SAMHSA is requesting $12.0 million for the *Preventing Prescription Drug/Opioid Overdose-Related Deaths* (PDO II) program, authorized in CARA. FY 2018 is the first-time appropriations for this newly-authorized program will be requested. The purpose of this program is to reduce the number of prescription drug/opioid overdose-related deaths and adverse events among individuals at risk for OUD. Applicants will train first responders and members of other key community sectors at the state, local government, and tribal levels to implement secondary prevention strategies, such as the administration of naloxone through FDA-approved delivery devices to reverse the effects of opioid overdose.

SAMHSA is also requesting $1.0 million to support a new cohort of grants through the *Building Communities of Recovery* program. This program mobilizes resources within and outside of the recovery community to increase the prevalence and quality of long-term recovery support for people with SUDs. These grants support the development, enhancement, expansion, and delivery of recovery support services, as well as promotion of and education about recovery.

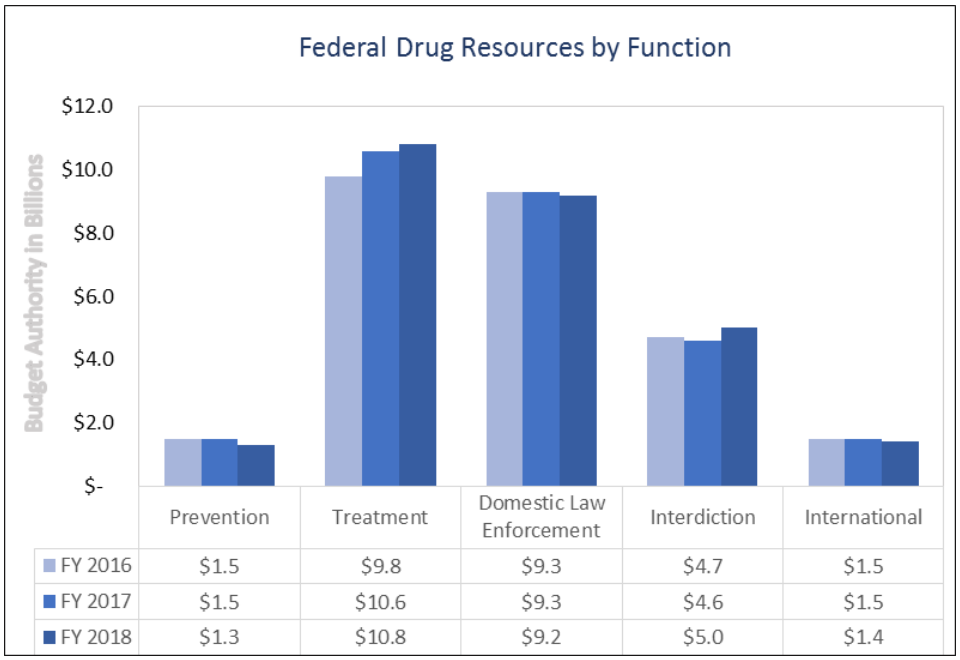
At the DOJ, the Office of Justice Programs is requesting $20.0 million for grants under the *Comprehensive Opioid Abuse Program*. This new program aims to support cross-system collaboration; develop and implement strategies to reach survivors of non-fatal overdoses and their loved ones; provide treatment and recovery support services; expand diversion and alternative to incarceration programs; expand services in rural or tribal communities; implement and enhance PDMPs; and assess the impact of new strategies.

At the VA, $50 million authorized under CARA is being requested for activities to increase opioid safety practices and improve care for Veterans within the Veterans Health Administration. VA began implementation of these activities with CR funds in FY 2017.

21st Century Cures Act

The *21st Century Cures Act* provides a total of $970 million over two fiscal years (FY 2017 and FY 2018) to HHS to address the opioid crisis by increasing treatment, reducing unmet treatment need, and reducing opioid overdose related deaths through the provision of prevention, treatment, and recovery activities for OUD (including prescription opioids, as well as illicit drugs such as heroin).

SAMHSA is administering the *21st Century Cures Act* funding through the *State Targeted Response to the Opioid Crisis Grants*. The President's Budget requests $500 million for state grants under this program. Grantees use epidemiological data to drive decision-making, rapidly address gaps in their systems of care, implement prevention strategies, deliver RSSs, and report progress on expanding treatment and reducing opioid overdose deaths.



	Prevention	Treatment	Domestic Law Enforcement	Interdiction	International
FY 2016	$1.5	$9.8	$9.3	$4.7	$1.5
FY 2017	$1.5	$10.6	$9.3	$4.6	$1.5
FY 2018	$1.3	$10.8	$9.2	$5.0	$1.4

Figure 6. Drug Resources by Function

FY 2018 Consolidated Federal Drug Control Budget

The consolidated National Drug Control Budget details agency resources by function. Functions categorize the activities of agencies into common drug control areas. Figure 6 details funding by function.

Prevention

Preventing drug use before it starts is a fundamental element of a comprehensive approach to drug control. Federal resources totaling $1.3 billion in support of education and outreach programs has been requested to educate young people about the consequences of drug use and prevent youth initiation. This represents a decrease of $167.5 million (11.1%) over the FY 2017 level; the major efforts are highlighted below:

Substance Abuse Prevention and Treatment Block Grant ($370.9 million)
Department of Health and Human Services – Substance Abuse and Mental Health Services Administration
Twenty percent of the $1.9 billion (i.e., $370.9 million) Substance Abuse Prevention and Treatment Block Grant is the minimum set aside to support prevention services. State Substance Abuse Administering Agencies use these funds to develop infrastructure and capacity specific to SUD prevention. Some State Substance Abuse Administering Agencies rely heavily on the 20% set-aside to fund prevention, target gaps in prevention services, and enhance existing program efforts.

Education's Prevention Efforts ($48.9 million)
Department of Education
The $48.9 million request includes $46.3 million for School Climate Transformation Grants and related technical assistance. These funds help create positive school climates through multi-tiered decision-making frameworks that guide the selection, integration, and implementation of the best evidence-based behavioral practices. A key aspect of this multi-tiered approach is that it provides differing levels of support and interventions to students based on their needs. In schools where these frameworks are implemented well, there is evidence that youth risk factors are improved; improved risk factors are correlated with reduced drug use, among other improved behaviors.

***Prevention* Research ($331.9 million)**
Department of Health and Human Services – National Institutes of Health
NIH's NIDA invests in genetics, neuroscience, pharmacotherapy, and behavioral and health services research, producing innovative strategies for preventing SUDs. In addition, NIDA is supporting research to better understand the impact of changes in state policies related to marijuana. Through NIAAA, the NIH helps to develop strategies to prevent the short- and long-term consequences of alcohol use among youth.

Drugged Driving ($2.72 million)
Department of Transportation, National Highway Traffic Safety Administration
NHTSA's FY 2018 request supports the Drug-Impaired Driving Program, which provides public information, outreach efforts, and improved law enforcement training to help reduce drugged driving. Funding will also allow NHTSA to continue to conduct research designed to reduce the incidence of drug-impaired driving.

Anti-Doping Activities/World Anti-Doping Agency Dues ($11.8 million)
Office of National Drug Control Policy
Anti-doping activities focus on efforts to educate athletes on the dangers of drug use, eliminate doping in amateur athletic competitions, and rely on standards established and recognized by the United States Olympic Committee. Funding for both efforts promotes an increased awareness in the United States and internationally of the health and ethical dangers of illicit drug use and doping in sport. Funding and participation in the Anti-Doping Activities/World Anti-Doping Agency is necessary to compete in international events. These activities support state-of-the-art research within the scientific and public health communities, while striving to protect athletes' fundamental rights to participate in drug-free sports, and thus promote the health and safety of athletes at all levels.

Treatment and Recovery

Treatment and recovery support services are essential elements of reducing drug use and its consequences. The FY 2018 Budget proposes $10.8 billion, an increase of $202.6 million (1.9%) over the FY 2017 annualized CR level in federal funds for early intervention, treatment, and recovery services. SUD treatment services need to be integrated better into primary care settings, made more widely accessible, and made eligible for insurance coverage on par with other medical conditions. The major efforts in this area include the following:

Medicare- & Medicaid-funded Substance Abuse Treatment Services ($5,840.0 million)
Department of Health and Human Services – Centers for Medicare & Medicaid Services
SUD treatment is usually financed through a variety of public and private sources (i.e., private health insurance, Medicaid, Medicare, state and local funds, and other federal support). The Federal Government makes its largest contribution to the payment for treatment through the Medicaid and Medicare programs. The Medicaid estimate is based on federal reimbursement to states for SUD treatment services. Medicare supports treatment for SUDs in both inpatient and outpatient settings.

Substance Abuse Treatment for Veterans ($721.7 million)
Department of Veterans Affairs – Veterans Health Administration
The Department of Veterans Affairs (VA) operates a national network of SUD treatment programs located in the Department's medical centers, residential rehabilitation facilities, and outpatient clinics. It provides effective, safe, efficient, recovery-oriented, and compassionate care for Veterans with SUDs and mental illness.

Substance Abuse Prevention and Treatment Block Grant ($1,483.8 million)
Department of Health and Human Services – Substance Abuse and Mental Health Services Administration
Up to 80% of the $1.9 billion Substance Abuse Prevention and Treatment Block Grant (i.e., $1,483.8 million) is estimated to support treatment services and related activities. This formula-based funding to states supports the provision of SUD treatment services, providing maximum flexibility to states to respond to their local and/or regional emergent issues impacting health, public health, and public safety through a consistent federal funding stream. The grant allows states to provide a range of clinical and recovery support services to clients during treatment and recovery, and supports planning, coordination, needs assessment, and quality assurance.

Screening, Brief Intervention, and Referral to Treatment ($46.8 million)
Department of Health and Human Services – Substance Abuse and Mental Health Services Administration
The SBIRT program, funded via Public Health Service Evaluation funds, provides grants to health care providers to intervene early in the disease process before individuals achieve dependency, and to motivate the clients with SUDs to engage in SUD treatment. Grant funds will further integrate Screening, Brief Intervention, and Referral to Treatment within medical treatment settings to provide early identification and intervention to at-risk individuals within the context of their primary care provider.

Treatment Research ($575.8 million)
Department of Health and Human Services – National Institutes of Health
NIH's NIDA invests in genetics, neuroscience, pharmacotherapy, and behavioral and health services research, producing innovative strategies for treating SUDs. For example, NIDA supports a large research network for conducting studies related to treatment of SUDs in the criminal justice system, including studies that pertain to the implementation of MAT and seek, test, treat, and retain for individuals with SUDs at risk for HIV. Through NIAAA, the NIH helps to develop strategies to treat the short- and long-term consequences of alcohol misuse among youth.

Substance Use Disorders Treatment for Military Service Members/Families ($76.7 million)
Department of Defense – Defense Health Program
DOD's Defense Health Program provides medical and dental services, including treatment for SUDs, for all members of the armed forces to include all eligible beneficiaries, including military family members. In addition to treatment services, the Defense Health Program also conducts alcohol and SUD research.

Homeless Assistance Grants - Continuum of Care ($494.2 million)
Department of Housing and Urban Development
The *Strategy* calls for federal support for reducing barriers to recovery from SUDs, including lack of housing. For persons in recovery, structured and supportive housing promotes healthy recovery outcomes. The Department's Continuum of Care—Homeless Assistance Grants support efforts to eliminate homelessness by financing local solutions to locate, intervene, and house the homeless population. These programs provide housing and supportive services on a long-term basis.

Drug Courts ($99.9 million)
Department of Health and Human Services - Substance Abuse and Mental Health Services Administration
Department of Justice - Office of Justice Programs
Drug courts help reduce recidivism, provide treatment to individuals with SUDs, and improve the likelihood of successful rehabilitation through early, continuous, and intense judicially supervised treatment, mandatory periodic drug testing, community supervision, appropriate sanctions, and other rehabilitation services. HHS ($59.9 million) and DOJ ($40.0 million), work together to enhance court services, coordination, and the SUD treatment capacity of juvenile, family and adult drug courts.

Bureau of Prisons Drug Treatment Efforts ($119.1 million)
Department of Justice, Bureau of Prisons
BOP continues to develop evidence-based treatment practices to manage and treat incarcerated individuals with SUDs. BOP's strategy includes early identification through psychological screening of individuals entering prison. According to the severity of the disease, BOP provides drug education, treatment for those within the general population, separate intensive residential SUD treatment and community transition treatment. The request includes $1.0 million to expand BOP's MAT field trial program, which provides medication during the last two months of incarceration and for four to six weeks after release in community custody, a residential reentry center, or home confinement.

Judiciary Treatment Efforts ($172.8 million)
Federal Judiciary
The Federal Judiciary provides for court-ordered drug testing, drug treatment, and supervision of federal defendants, probationers, parolees, and those on supervised release after incarceration. Funding is used by the probation and pretrial services offices for drug testing and treatment of federal defendants and offenders. Probation and pretrial services officers have primary responsibility for enforcing conditions of release imposed by the courts and for monitoring the behavior of persons placed under their supervision. With Executive Office of the U.S. Attorneys oversight, officers administer a program of drug testing and treatment for persons on pretrial release, probation, supervised release after incarceration, and parole. The goal is to eliminate

substance use by persons under supervision and to remove violators from the community before relapse leads to recidivism.

Domestic Law Enforcement

Maximizing federal support for interagency law enforcement drug task forces is critical to leveraging limited resources. A total of $9.2 billion in federal resources are requested in FY 2018 to support domestic law enforcement efforts (including state and local assistance, as well as federal investigation, prosecution, and corrections), a decrease of $62.7 million (0.7%) below the FY 2017 annualized CR level. The major efforts are highlighted below.

Methamphetamine Enforcement and Lab Cleanup Grants ($11.0 million)
Department of Justice
These grants aid state, local, and tribal law enforcement agencies in support of programs to address methamphetamine production and distribution. Working with the DEA, funding also supports assistance to state and local law enforcement in removing and disposing of hazardous materials generated by clandestine methamphetamine labs, and providing training, technical assistance, and equipment to assist law enforcement agencies in managing hazardous waste.

Federal Law Enforcement Training Center ($48.8 million)
Department of Homeland Security
The Federal Law Enforcement Training Center (FLETC) is a law enforcement training facility that provides training and technical assistance to federal, state, local, tribal, territorial, and international law enforcement entities. As part of its curriculum, FLETC provides training programs comprised of drug enforcement activities and drug-related investigations to enhance the qualifications of law enforcement personnel.

Federal Drug Investigations ($3,359.8 million)
Multiple agencies
Federal law enforcement personnel—including those from DOJ ($2,582.2 billion), DHS ($490.9 million), Treasury ($60.3 million), Interior ($14.9 million), and Agriculture ($14.6 million) - prepare drug cases for the arrest and prosecution of leaders and traffickers of illegal drug organizations, seize drugs and assets, and enforce federal laws and regulations governing the legitimate handling, manufacturing, and distribution of controlled substances.

Federal Prosecution ($842.4 million)
Multiple agencies
Several agencies— (including DOJ's Organized Crime Drug Enforcement Task Force Program ($161.3 million), U.S. Marshals Service ($129.8 million), Executive Office of the U.S. Attorneys ($78.1 million), Criminal Division ($37.7 million), and the Federal Judiciary ($435.5 million)— conduct Federal criminal proceedings against drug trafficking and money laundering organizations. The related costs include salaries for attorneys and other court personnel, defender services, judicial and courthouse security, prisoner security, and other administrative costs.

Corrections ($4,410.4 million)
Department of Justice/Federal Judiciary
The BOP ($3,284.7 million), the Federal Judiciary ($597.0 million), and the U.S. Marshals Service ($528.6 million) conduct activities associated with the incarceration and/or monitoring of drug-related offenders. The request includes funding for the costs associated with inmate care, security and facility maintenance, contracted confinement, and general management and administration.

Interdiction

The United States continues to face a serious challenge from the large-scale smuggling of drugs from abroad that are distributed to every region of the Nation. In FY 2018, the Administration's request includes $5.0 billion to support the efforts of federal law enforcement agencies, the military, the intelligence community, and our international allies to support collaboration to interdict or disrupt shipments of illegal drugs, their precursors, and their illicit proceeds. The FY 2018 request represents an increase of $453.4 million, (9.9%) above the FY 2017 annualized CR level. The major efforts are highlighted below.

Customs and Border Protection ($3,118.7 million)
Department of Homeland Security
CBP implements border enforcement strategies to interdict and disrupt the flow of narcotics and other contraband across our Nation's borders. The comprehensive interdiction strategy includes the border security personnel at and between ports of entry, detection and monitoring provided by aviation assets, and border security infrastructure and technology.

United States Coast Guard ($1,452.7 million)
Department of Homeland Security
One facet of the United States Coast Guard's (USCG) mission is maritime interdiction. The USCG functions as the maritime counternarcotics presence in the source, transit, and arrival zones. Their maritime interdiction activities disrupt the flow of drugs into the United States.

Federal Aviation Administration Interdiction Support ($13.2 million)
Department of Transportation/Federal Aviation Administration
Air traffic controllers staffing Air Route Traffic Control Centers monitor the Air Defense Identification Zones to detect possible suspicious aircraft movement. When suspicious movement is identified, the Federal Aviation Administration (FAA) notifies the DEA and USCG of such activity. Upon confirmation of suspicious aircraft movement, FAA controllers support interdiction efforts by providing radar vectors to track the time of arrival, traffic advisory information, and last known positions to intercept aircrafts of interest.

Department of Defense Drug Interdiction ($413.2 million)
Department of Defense
DOD's counterdrug programs detect, monitor, and support the disruption of drug trafficking organizations. Additionally, DOD coordinates interagency resources and force requirements of air and surface assets in the Western Hemisphere Transit Zone.

International Efforts

Illicit drug production and trafficking generate huge profits and are responsible for the establishment of criminal enterprise networks that are powerful and corrosive forces that destroy the lives of individuals, tear at the social fabric, and weaken the rule of law in affected countries. In FY 2018, $1.4 billion is requested for international drug control efforts, a decrease of $146.1 million (9.6%) below the FY 2017 annualized CR level. These funds are requested to support the efforts of the United States Government and our international partners around the globe to meet the challenges of illicit trafficking of all drugs, including synthetics and precursors, and illicit substance use. The major efforts in this area include the following.

DEA's International Efforts ($470.4 million)
Department of Justice
The focus of DEA's international enforcement program is to disrupt or dismantle the most significant international drug and precursor chemical trafficking organizations around the world. Personnel in DEA's foreign country offices focus their investigative efforts on the most significant international command and control organizations threatening the United States. DEA coordinates all programs involving drug law enforcement in foreign countries, and provides intelligence to assist the interagency community in determining future trends in drug trafficking and evaluating their long-term impact. DEA works closely with the United Nations, Interpol, and other organizations on matters relating to international drug and chemical control programs.

Bureau of International Narcotics and Law Enforcement Affairs ($290.3 million)
Department of State
In support of the *Strategy*, Bureau of International Narcotics and Law Enforcement Affairs (INL) works closely with partner nations and source countries to disrupt illicit drug production, strengthen criminal justice systems and law enforcement institutions, and combat transnational organized crime. INL is comprehensive in its approach to the counterdrug mission and provides training and technical assistance for prevention and treatment programs.

United States Agency for International Development ($83.6 million)
Department of State
The United States Agency for International Development (USAID) provides foreign assistance funds to develop holistic alternatives to illicit drug production by providing agricultural assistance, improving small scale infrastructure, increasing market accessibility, and incentivizing licit crop production. USAID's alternative development programs foster economic growth, local governance and civil society strengthening, and enhanced security of impacted communities.

DOD International Counternarcotics Efforts ($491.1 million)
Department of Defense
The international support programs of DOD's Combatant Commands detect, interdict, disrupt, or monitor activities related to drug trafficking organizations and transnational criminal organizations. In the Western Hemisphere Transit Zone, DOD functions as the command and control support for counterdrug activities for federal, state, local and international partners.

Table 3. Federal Drug Control Spending by Function, FY 2016 – FY 2018 (Budget Authority in Millions)

		FY 2016 Final	FY 2017 CR	FY 2018 Request	FY17 - FY18 Change Dollars	FY17 - FY18 Change Percent
Function						
	Treatment	$9,845.1	$10,580.8	$10,783.4	$202.6	*1.9%*
	Percent	*36.6%*	*38.5%*	*38.9%*		
	Prevention	1,486.4	1,507.4	1,339.9	-167.5	*-11.1%*
	Percent	*5.5%*	*5.5%*	*4.8%*		
	Domestic Law Enforcement	9,282.8	9,298.6	9,235.8	-62.8	*-0.7%*
	Percent	*34.5%*	*33.8%*	*33.3%*		
	Interdiction	4,734.7	4,569.0	5,022.4	453.4	*9.9%*
	Percent	*17.6%*	*16.6%*	*18.1%*		
	International	1,524.9	1,521.0	1,375.0	-146.1	*-9.6%*
	Percent	*5.7%*	*5.5%*	*5.0%*		
Total		**$26,874.0**	**$27,476.8**	**$27,756.5**	**$279.7**	***1.0%***
Supply/Demand						
	Demand Reduction	$11,331.5	$12,088.2	$12,123.3	$35.1	*0.3%*
	Percent	*42.2%*	*44.0%*	*43.7%*		
	Supply Reduction	15,542.5	15,388.6	15,633.2	244.6	*1.6%*
	Percent	*57.8%*	*56.0%*	*56.3%*		
Total		**$26,874.0**	**$27,476.8**	**$27,756.5**	**$279.7**	***1.0%***

Table 4. Federal Drug Control Spending by Agency (Budget Authority in Millions)

	FY 2016 Final	FY 2017 CR	FY 2018 Request
Department of Agriculture			
U.S. Forest Service	12.3	12.9	15.6
Court Services and Offender Supervision Agency for the District of Columbia	55.4	55.3	56.1
Department of Defense			
Drug Interdiction and Counterdrug Activities[1] (incl. OPTEMPO, DSCA, and OCO)	1,302.8	1,299.4	1,127.8
Defense Health Program	76.7	75.8	76.7
Total DoD	**1,379.5**	**1,375.1**	**1,204.6**
Department of Education			
Office of Elementary and Secondary Education	50.3	49.1	48.9
Federal Judiciary	1,147.8	1,166.7	1,210.9
Department of Health and Human Services			
Administration for Children and Families	18.5	18.6	20.0
Centers for Disease Control and Prevention	75.6	75.4	75.4
Centers for Medicare & Medicaid Services[2]	5,390.0	5,550.0	5,840.0
Health Resources and Services Administration	119.0	121.0	171.0
Indian Health Service	104.7	104.9	105.1
National Institute on Alcohol Abuse and Alcoholism	55.2	55.2	42.7
National Institute on Drug Abuse	1,049.0	1,075.4	865.0
Substance Abuse and Mental Health Services Administration[3]	2,533.7	3,052.1	2,943.2
Total Health and Human Services	**9,345.7**	**10,052.7**	**10,062.5**
Department of Homeland Security			
Customs and Border Protection	2,687.2	2,663.7	3,118.7
Federal Emergency Management Agency	8.3	8.3	6.2
Federal Law Enforcement Training Center	44.1	43.9	49.3
Immigration and Customs Enforcement	508.9	514.7	524.6
United States Coast Guard	1,597.1	1,456.0	1,452.7
Total Homeland Security	**4,845.6**	**4,686.4**	**5,151.5**
Department of Housing and Urban Development			
Community Planning and Development	490.5	489.5	494.2
Department of the Interior			
Bureau of Indian Affairs	9.7	9.7	9.3
Bureau of Land Management	5.1	5.1	5.1
National Park Service	3.5	3.3	3.3
Total Interior	**18.3**	**18.1**	**17.7**

	FY 2016 Final	FY 2017 CR	FY 2018 Request
Department of Justice			
Assets Forfeiture Fund	258.4	230.1	227.5
Bureau of Prisons[4]	3,532.6	3,526.0	3,403.8
Criminal Division	39.0	38.0	37.7
Drug Enforcement Administration	2,425.5	2,433.4	2,583.6
Organized Crime Drug Enforcement Task Force Program	512.0	511.0	526.0
Office of Justice Programs	278.2	297.7	240.2
U.S. Attorneys	72.6	72.6	78.1
U.S. Marshals Service	771.3	792.8	812.8
Total Justice	**7,889.7**	**7,901.7**	**7,909.7**
Department of Labor			
Employment and Training Administration	5.7	6.0	6.0
Office of National Drug Control Policy			
High Intensity Drug Trafficking Areas	250.0	249.5	246.5
Other Federal Drug Control Programs	109.8	109.6	103.7
Salaries and Expenses	20.0	20.0	18.4
Total ONDCP	**379.9**	**379.1**	**368.6**
Department of State[5]			
Bureau of International Narcotics and Law Enforcement Affairs	405.3	404.5	290.3
United States Agency for International Development	70.5	70.4	83.6
Total State	**475.8**	**474.9**	**373.9**
Department of Transportation			
Federal Aviation Administration	30.4	31.6	31.7
National Highway Traffic Safety Administration	3.5	2.7	2.7
Total Transportation	**33.8**	**34.3**	**34.4**
Department of the Treasury			
Internal Revenue Service	60.3	60.3	60.3
Department of Veterans Affairs			
Veterans Health Administration	683.4	714.6	741.7
Total Federal Drug Budget	**$26,874.0**	**$27,476.8**	**$27,756.5**

1. Due to statutory changes included in the FY 2017 National Defense Authorization Act that consolidated the DOD's security sector assistance authorities, funding for building foreign partner counter-drug enforcement capacities is now included in DOD's Defense Security Cooperation Agency's budget request.
2. The estimates for the CMS reflect Medicaid and Medicare benefit outlays (excluding spending under Medicare Part D) for substance use disorder treatment; they do not reflect budget authority. The methodology for Medicaid estimates has been refined from prior years to more accurately reflect spending. The estimates were developed by the CMS Office of the Actuary.
3. Includes budget authority and funding through evaluation set-aside authorized by Section 241 of the Public Health Service (PHS) Act.
4. Funding for the FY 2018 column excludes a proposed rescission of unobligated balances.
5. Funding for 2017 column is a mechanical calculation that does not reflect decisions on funding priorities.
6. Detail may not add due to rounding

PRESIDENT'S COMMISSION ON COMBATING DRUG ADDICTION AND THE OPIOID CRISIS

Commission Charter

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1. **Committee's Official Designation:** President's Commission on Combating Drug Addiction and the Opioid Crisis (Commission).

2. **Authority:** The Commission is being established in accordance with Executive Order No. 13784 of March 29, 2017, and the provisions of the Federal Advisory Committee Act (FACA), as amended, 5 U.S.C. App. 2.

3. **Objectives and Scope of Activities:** The Commission is established in the interest of obtaining advice and recommendations for the President regarding the opioid crisis. The Commission will function solely as an advisory body and will make recommendations regarding policies and practices for combating drug addiction with particular focus on the current opioid crisis in the United States. The heads of executive departments and agencies shall, to the extent permitted by law, provide the Commission with information concerning drug addiction and the opioid crisis when requested. To achieve this goal, the Commission shall:
    a. identify and describe the existing Federal funding used to combat drug addiction and the opioid crisis;
    b. assess the availability and accessibility of drug addiction treatment services and overdose reversal throughout the country and identify areas that are underserved;
    c. identify and report on best practices for addiction prevention, including healthcare provider education and evaluation of prescription practices, collaboration between State and Federal officials, and the use and effectiveness of State prescription drug monitoring programs;
    d. review the literature evaluating the effectiveness of educational messages for youth and adults with respect to prescription and illicit opioids;
    e. identify and evaluate existing Federal programs to prevent and treat drug addiction for their scope and effectiveness, and make recommendations for improving these programs; and
    f. make recommendations to the President for improving the Federal response to drug addiction and the opioid crisis.

4. **Description of Duties:** The duties of the Commission are solely advisory.

5. **Agency or Official to Whom the Committee Reports:** The Commission shall provide its formal interim and final findings and recommendations to the President. The Commission shall report to the President, directly at meetings with the President and also through the Director of National Drug Control Policy.

6. **Agency Responsible for Providing Necessary Support:** The Office of National Drug Control Policy (ONDCP) within the Executive Office of the President will provide necessary administrative support for the Commission with the approval of the Director of ONDCP and will maintain staff and quarters to meet the needs of the Commission. The Director of ONDCP will be responsible for ensuring that the requirements of §6(b) of FACA are fulfilled.

7. **Estimated Annual Operating Costs and Staff Years:** To be determined.

8. **Designated Federal Officer:** The Designated Federal Officer (DFO) will be a full-time officer or employee of the Federal Government appointed by the Director of ONDCP or the President. The DFO will approve or call all of the Commission's meetings, prepare all meeting agendas, attend all meetings, and adjourn any meeting when the DFO determines adjournment to be in the public interest. Should the Commission Chair designate any subcommittees, the DFO will similarly approve or call any/all subcommittee meetings, prepare all subcommittee meeting agendas, attend all such meetings, and adjourn any subcommittee meeting when the DFO determines adjournment to be in the public interest.

9. **Estimated Number and Frequency of Meetings:** The Commission shall meet as frequently as needed and called and approved by the DFO. As required by FACA, the Commission will hold open meetings unless it is determined by the Executive Director that a meeting or a portion of a meeting may be closed to the public in accordance with subsection (c) of section 552b of Title 5, United States Code. Interested persons may attend meetings, appear before the Commission, and file statements with the Commission.

10. **Duration and Termination:** Within 90 days of the date of the Executive Order establishing this Commission, the Commission shall submit to the President a report of the Commission's interim findings and recommendations regarding how the Federal government can address drug addiction and the opioid crisis. The Commission shall submit to the President a report of final findings and recommendations on or before October 1, 2017, unless the Commission Chair provides written notice to the President that an extension of time is necessary. The Commission shall terminate thirty (30) days after it presents its final report to the President, unless the Commission's term is extended by the President prior to that date.

11. **Membership:** The Commission shall be composed of members appointed by the President. As required by FACA, the membership of the Commission will be fairly balanced in terms of the points of view represented and the functions to be performed by the Commission. The advice and recommendations of the Commission will be the result of the Commission's independent judgment. The President shall designate a Chair of the Commission (Commission Chair or Chair) from among the Commission's members. The Director of ONDCP will designate an Executive Director of the Commission who is a full-time employee from ONDCP who will supervise staff and coordinate administrative support for

the Commission. The Executive Director will work at the direction of the Chair on all Commission related matters and will attend each meeting of the Commission. Members serve at the pleasure of the President.

12. **Subcommittees:** Subcommittees composed of members designated by the Chair may be established by the Chair in consultation with the Executive Director and the DFO to perform specific functions within the Commission's jurisdiction. The Chair will notify the Executive Director and the DFO upon the establishment of each subcommittee and will provide the Executive Director and the DFO with information on its name, membership, function, and estimated frequency of meetings. Subcommittees must not incur costs or expenses without prior consultation with the Executive Director and express written authorization of the Chair. Subcommittees must not provide any information to any entity without written authorization of the Chair. Subcommittees are required to report any findings, conclusions, or recommendations to the Commission and must not provide any information directly to the President.

13. **Recordkeeping:** The records of the Commission and its subcommittees will be handled in accordance with General Records Schedule 6.2 and approved agency records disposition schedules. These records will be available for public inspection and copying, subject to the Freedom of Information Act, 5 U.S.C. § 552.

14. **Filing Date:** The filing date of this charter is April 24, 2017.

Approved on this 24th day of April, 2017

Richard J. Baum, Acting Director

Office of National Drug Control Policy

Appendices

Appendix 1. Acronyms

ACA:	Affordable Care Act
ADAM:	Arrestee Drug Abuse Monitoring Program
AED:	Advanced Electronic Data
AUD:	alcohol use disorder
AHRQ:	Agency for Healthcare Research and Quality
ASAM:	American Society of Addiction Medicine
BJA:	Bureau of Justice Assistance
BOP:	Bureau of Prisons
CARA:	Comprehensive Addiction and Recovery Act
CBP:	U.S. Customs and Border Protection
CDC:	Centers for Disease Control and Prevention
CHW:	community health worker
CME:	continuing medical education
CMS:	Centers for Medicare and Medicaid Services
CRP:	collegiate recovery programs
DAWN:	Drug Abuse Warning Network
DEA:	Drug Enforcement Administration
DHS:	Department of Homeland Security
DOD:	Department of Defense
DOE:	Department of Education
DOJ:	Department of Justice
DOL:	Department of Labor
DOT:	Department of Transportation
DTO:	Drug Trafficking Organization
ED:	Emergency Department
EHR:	electronic health records
EMR:	emergency medical responder
EMS:	emergency medical services
EMT:	emergency medical technician
EMTALA:	Emergency Medical Treatment and Labor Act
EPCS:	electronic prescribing of controlled substances
ER:	extended-release
FAA:	Federal Aviation Administration

FDA:	U.S. Food and Drug Administration
FLETC:	Federal Law Enforcement Training Center
HCAHPS:	Hospital Consumer Assessment of Healthcare Providers and Systems
HCPCS:	Healthcare Common Procedure Coding System
HCV:	hepatitis C virus
HHS:	U.S. Department of Health and Human Services
HIDTA:	High Intensity Drug Trafficking Areas
HIV:	human immunodeficiency virus
HRSA:	Health Resources and Services Administration
HUD:	heroin use disorder
IMD:	Institutes of Mental Disease
IMF:	USPS International Mail Facilities
INL:	Bureau of International Narcotics and Law Enforcement Affairs
IR:	immediate-release
MAT:	Medication-Assisted Treatment
MDI:	medicolegal death investigation
ME/C:	medical examiners and coroners
MHPAEA:	Mental Health Parity and Addiction Equity Act
NARR:	National Alliance for Recovery Residents
NASEM:	National Academies of Sciences, Engineering, and Medicine
NAS:	neonatal abstinence syndrome
NHTSA:	National Highway Traffic Safety Administration
NIAAA:	National Institute on Alcohol Abuse and Alcoholism
NIC:	National Institute on Corrections
NIDA:	National Institute on Drug Abuse
NIH:	National Institutes of Health
NQTL:	non-quantitative treatment limits
NSC:	National Security Council
NSDUH:	National Survey on Drug Use and Health
NPS:	new psychoactive substances
ONDCP:	Office of National Drug Control Policy
OTP:	opioid treatment programs
OUD:	opioid use disorder
PDMP:	prescription drug monitoring program
RCO:	recovery community organization
RSS:	recovery support services

SAMHSA:	Substance Abuse and Mental Health Services Administration
SBIRT:	Screening, Brief Intervention, and Referral to Treatment
SUD:	substance use disorder
USAID:	United States Agency for International Development
USCG:	United States Coast Guard
USPS:	United States Postal Service
USPIS:	United States Postal Inspection Service
USPSTF:	United States Preventative Services Task Force
VA:	Department of Veteran Affairs
VBP:	Value-Based Purchasing

Appendix 2. History of Opiate Use and Abuse

The opium poppy was a medicinal plant used by ancient civilizations. It blunted pain; elevated mood; relaxed; dulled stress, melancholy, and anxiety; and induced sleep. With the dawning of modern chemistry in the early 1800's, morphine, codeine, and thebaine were purified from the opium poppy *Papaver somniferum,* and their chemical structures identified. Scientific curiosity or optimization of medicinal properties drove chemists to synthesize variations of these naturally occurring opioids. The end products included heroin, oxycodone, oxymorphone, hydrocodone, hydromorphone, and others.

To avoid reliance on the poppy plant for opioids, *de novo* compounds such as methadone, meperidine, fentanyl, tramadol, U47700, were subsequently created. These drugs were structurally distinct from morphine yet targeted the same pain-reducing/pleasure-inducing receptors/circuits as plant-derived morphine analogs to engender pain relief, suppression of cough and intestinal function and chemical coping of psychological distress. Susceptible individuals, whether medical or non-medical users discovered the euphoriant properties of potent opioids delivered rapidly into the brain, especially by smoking or injection.

Opioid mechanisms. Opioid analgesics target opioid signaling systems within circuits engaged in diverse homeostatic mechanisms, especially management of pain, anxiety, stress, intestinal motility, cough mechanisms and hedonic pleasure. Opioid signaling is comprised of endogenous chemical neurotransmitters (small and large mobile peptides such as endorphins that transmit signals) and their corresponding opioid receptors (large anchored proteins that interpret signals). These signaling systems are widely distributed throughout the human brain and body. Three major opioid receptors (μ or mu, κ or kappa, and δ or delta), their subtypes and splice variants have been identified. Opioids activate one or more of these G-protein–coupled transmembrane molecules, to trigger diverse responses governed by splice variants, post-translational modifications, and receptor heterodimer or homodimer formation.[258] All exogenous opioids that target the μ-opioid receptor suppress pain perception, slow gastrointestinal motility, attenuate cough, and induce pleasurable sensations or intense euphoria. At sufficiently high doses, activation of μ-opioid receptors in the brain stem can depress respiration, leading to reduced blood flow and oxygen in the brain and even death. Frequent exposure to opioids leads to tolerance, a diminution of specific signaling functions of the mu opioid receptor (e.g., euphoria and respiratory depression), which may drive the user to escalate drug doses to levels that can be fatal in the drug-naïve or in abstinent former users. If high dose opioids are reintroduced during abstinence (e.g. released prisoners or in long term recovery), the risk of a lethal overdose is grave as tolerance to opioids wanes during abstinence.

Historical Origins of Iatrogenic Opioid Addiction. In the mid- to late-19th century, opioid use rose dramatically, fueled by physicians' unrestrained opioid prescriptions (morphine, laudanum, paregoric, codeine, heroin) for pain or other ailments, by inclusion of opioids in aggressively promoted patent medicines, and by liberal use of opioid-based treatments for injuries and diseases gnawing at Civil War combatants and veterans. Opioids were undoubtedly more effective and reliable medications for a variety of ailments, compared with existing alternatives. During this first wave, physicians were largely responsible for iatrogenic addiction to opioids among patients. By 1900, 1 in 200 people were addicted in the United States. In parallel with clinicians and pharmacists issuing unrestrained opioid supplies to treat medical ailments and addiction, profiteers organized clandestine, illicit opioid distribution networks. Powered by unregulated international

production and shipments of opium, opium dens proliferated in the United States and created a non-medical, addicted population among denizens of these sites.[259,260,261] The steep rise in consumption of medical opioids or smoked opium led to an alarming surge of addictions, either medically-induced, or resulting from opium smoking. The two populations did not "cross-over," nor merge regarding drug sources, types of opioids, or routes of administration. This nation-wide crisis extended across socio-economic strata, and reached urban and rural areas. Thereafter, smaller scale waves of heroin addiction surfaced periodically during the 20th century, but these were confined to large cities.

Response to the First Crisis. Medical professionals, federal, local, and international regulatory bodies awakened to the epidemic of iatrogenic and situationally-based opioid addiction. One physician James F.A. Adams wrote compellingly on the adverse side effects of these medicinal drugs - depression, constipation, and the "opium habit," (addiction). Eventually, the first epidemic of opioid addiction was contained and then reversed by physicians, pharmacists, medical education, voluntary restraint, combined with federal regulations and law enforcement. In 1890, the U.S. government began taxing opium and by 1906, the Pure Food and Drug Act was passed, which required manufacturers to disclose the contents of their medicinal products to consumers. Three years later Congress passed the Opium Exclusion Act, banning its import for opium smoking. The International Opium Convention in the Hague and the Harrison Act of 1914 taxed and regulated the sale and distribution of opium and cocaine-based products, the first broadly based prohibition in American history. Opioids remained available for short-term medical use, but not for maintenance of addiction. Doctors and pharmacists who violated the Act, which discouraged morphine use to sustain addiction, were arrested. The United Nations Single Convention on Narcotic Drugs in 1961 and the Controlled Substances Act (CSA) of 1970 (Title II of the Comprehensive Drug Abuse Prevention and Control Act) established federal U.S. drug policy on regulating the manufacture, importation, possession, use and distribution of certain substances. The CSA was the national legislation for implementing the Single Convention on Narcotic Drugs. The DEA, the enforcement branch of the CSA, was charged with registration of physicians, stringent annual production quotas, chain-of-custody and other regulatory oversight.

Appendix 3. Interim Report, *President's Commission on Combating Drug Addiction and the Opioid Crisis*

Dear Mr. President:

I am proud to present to you today the interim report prepared by your Commission on Combating Drug Addiction and the Opioid Crisis. This interim report is just a start; our work is ongoing and we will have more to share with you and the nation later in the Fall of 2017. We now recommend several actions for you to take as our nation's Chief Executive and someone who spoke passionately on this issue in the 2016 campaign.

Our nation is in a crisis. Your Executive Order recognized that fact. The work of your Commission so far acknowledges the severity of this national problem.

According to the Centers for Disease Control (CDC), the most recent data estimates that 142 Americans die every day from a drug overdose. Our citizens are dying. We must act boldly to stop it. The opioid epidemic we are facing is unparalleled. The average American would likely be shocked to know that drug overdoses now kill more people than gun homicides and car crashes combined. In fact, between 1999 and 2015, more than 560,000 people in this country died due to drug overdoses – this is a death toll larger than the entire population of Atlanta. As we have all seen, opioids are a prime contributor to our addiction and overdose crisis. In 2015, nearly two-thirds of drug overdoses were linked to opioids like Percocet, OxyContin, heroin, and fentanyl. This is an epidemic that all Americans face because here is the grim reality: Americans consume more opioids than any other country in the world. In fact, in 2015, the amount of opioids prescribed in the U.S. was enough for every American to be medicated around the clock for three weeks.

Since 1999, the number of opioid overdoses in America have quadrupled according to the CDC. Not coincidentally, in that same period, the amount of prescription opioids in America have quadrupled as well. This massive increase in prescribing has occurred despite the fact that there has not been an overall change in the amount of pain Americans have reported in that time period. We have an enormous problem that is often not beginning on street corners; it is starting in doctor's offices and hospitals in every state in our nation.

But, the challenge of reducing opioid supplies has evolved. As access to prescription opioids tightens, consumers increasingly are turning to dangerous street opioids, heroin, fentanyl alone or combined, and mingled with cocaine or other drugs. In 2016, specific states witnessed an escalating number of overdose deaths due to heroin and/or fentanyl(s), in some states vastly exceeding deaths due to prescription opioids.

In 2015, 27 million people reported current use of illegal drugs or abuse of prescription drugs. Despite this self-reporting, only 10 percent of the nearly 21 million citizens with a substance use disorder (SUD) receive any type of specialty treatment according to the most recent National Survey on Drug Use and Health. This is contributing greatly to the increase of deaths from overdose.

Over forty percent of people with a substance use disorder also have a mental health problem, but less than half of these people receive treatment for either issue. The reasons for these treatment gaps are many, including lack of access to care, fear of shame and discrimination, and lack of motivation to seek treatment.

This Commission has been hard at work to meet the goals set for us in the Executive Order on March 29th, 2017. As a Commission, we have already met with leading national organizations in the addiction space, and we have received information and recommendations from countless individuals and groups, all of whom share in our commitment to beating this epidemic. The Commission thanks all the individuals and organizations, including Governors and representatives from Governors Offices from around the country, that have reached out to offer their experiences, expertise, and input.

In addition to conducting phone calls with Governors and their teams in all 50 states, we also held a listening session with bi-partisan members of Congress, and key cabinet members of your Administration. Individual Commission members have organized "listening sessions" and solicited recommendations from treatment providers, addiction psychiatrists and other physicians, data analysts, professional medical and treatment societies, medical educators, healthcare organizations, pharmacoepidemiologists, and insurance providers. Outreach also has been made to scientists with broad expertise in pain, addiction biology and treatment.

The first public meeting of the Commission was held on June 16th at the White House, and was a great success. The Commission members heard comprehensive public testimony by nine leading nonprofits, and have received more than 8,000 comments from the public, including comments from at least 50 organizations.

This information was reviewed by the Commission members and helped inform this interim report.

The first and most urgent recommendation of this Commission is direct and completely within your control. Declare a national emergency under either the Public Health Service Act or the Stafford Act. With approximately 142 Americans dying every day, America is enduring a death toll equal to September 11th every three weeks. After September 11th, our President and our nation banded together to use every tool at our disposal to prevent any further American deaths. Your declaration would empower your cabinet to take bold steps and would force Congress to focus on funding and empowering the Executive Branch even further to deal with this loss of life. It would also awaken every American to this simple fact: if this scourge has not found you or your family yet, without bold action by everyone, it soon will. You, Mr. President, are the only person who can bring this type of intensity to the emergency and we believe you have the will to do so and to do so immediately.

The Commission is additionally proposing the following recommendations for immediate action:

- **Rapidly increase treatment capacity. Grant waiver approvals for all 50 states to quickly eliminate barriers to treatment resulting from the federal Institutes for Mental Diseases (IMD) exclusion within the Medicaid program. This will immediately open treatment to thousands of Americans in existing facilities in all 50 states.**

  The Commission has been urged by every Governor, numerous treatment providers, parents, and non-profit advocacy organizations to eliminate the IMD exclusion within the Medicaid program. This component of the Social Security Act prohibits federal Medicaid funds from reimbursing services provided in an inpatient facility treating "mental diseases" (including SUDs) that have more than 16 beds. This exclusion makes states entirely responsible for Medicaid-eligible patients in inpatient treatment facilities, including patients undergoing withdrawal management in addiction treatment facilities rather than hospitals. The Commission members that serve as Governors, as well as individuals and organizations that treat Medicaid patients, are intimately aware of how the IMD exclusion impacts the ability to serve patients with severe SUDs that are best served in an inpatient setting. The Commission recognizes that legislation would be necessary to repeal the exclusion in its entirety. However, certainly after an emergency declaration by the President (and arguably even without it) the Department of Health and Human Services (HHS) Secretary would be empowered to immediately grant waivers to each state that requests one. This is the single fastest way to increase treatment availability across the nation.

- **Mandate prescriber education initiatives with the assistance of medical and dental schools across the country to enhance prevention efforts. Mandate medical education training in opioid prescribing and risks of developing an SUD by amending the Controlled Substance Act to require all Drug Enforcement Agency (DEA) registrants to take a course in proper treatment of pain. HHS should work with partners to ensure additional training opportunities, including continuing education courses for professionals.**

  According to a Substance Abuse and Mental Health Services Administration (SAMHSA) Center for Behavioral Health and Statistics Quality (CBHSQ) report, four out of every five new heroin users begin with nonmedical use of prescription opioids.

  In other words, Mr. President, this crisis began in our nation's health care system. While we acknowledge that some of this inappropriate overprescribing is done illegally and for profit, we believe the overwhelming percentage is due to a lack of education on these issues in our nation's medical and dental schools and a dearth of continuing medical education for practicing clinicians. This can and must be solved by using Presidential moral and legal authority to change this lack of education leading to addiction and death.

  There are several initiatives around the country aimed at ensuring that providers are aware of the potential for misuse and abuse of prescription opioids.

  Governor Baker's administration in Massachusetts has worked with the medical and dental schools in that state and the Medical Society to develop core competencies related to opioids and SUDs that all graduating students are expected to learn and put into practice. Other states such as Arizona, Connecticut, Pennsylvania, New York, and Utah have expanded

continuing medical education requirements for opioid prescribers and dispensers. Alternatively, the American Society of Addiction Medicine (ASAM) has recommended implementing a requirement that clinicians who apply for a registration with the DEA to prescribe controlled substances demonstrate competency in safe prescribing, pain management, and substance use identification. In New Jersey, Governor Christie recently signed a law that requires providers themselves to take continuing education related to opioids, and requires prescribers to discuss the risks of opioid dependence with their patients prior to the first prescription. We urge national implementation of these initiatives.

In our first Commission meeting, we heard from several nonprofits about the need to promote expanded implementation of the CDC *Guideline for Prescribing Opioids for Chronic Pain* through increased prescriber education initiatives. The Office of National Drug Control Policy (ONDCP) estimates that, apart from federal prescribers who are required to be trained, fewer than 20% of the over one million prescribers licensed to prescribe controlled substances to patients have training on how to prescribe opioids safely. Similarly, it seems that many medical providers are not well-versed on how to screen for addiction, and what to do if a patient has become dependent on substances or presents with an SUD. We urge you to instruct the Department of Justice (DOJ) and the DEA to require continuing medical education for every physician requesting an initial DEA license or the renewal of such a license.

The CDC and the U.S. Food and Drug Administration (FDA) should finalize, review and recommend national training standards working with the Accreditation Council for Continuing Medical Education (ACCME) to ensure training courses are coordinated with other federal agencies, professional societies, medical schools, and residency programs to avoid discrepancies.

The FDA should also work with the ACCME to develop data analytics to determine whether courses change practices, increase patient referrals to treatment, and methods to improve compliance consistent with opioid prescribing education.

Clinicians need more detailed and specific guidance on drug choice, dose, and quantity to be dispensed in treating specific pain conditions. We also recommend a detailed analysis of, and solutions to clinical problems encountered in applying recommended guidelines.

- **Immediately establish and fund a federal incentive to enhance access to Medication-Assisted Treatment (MAT). Require that all modes of MAT are offered at every licensed MAT facility and that those decisions are based on what is best for the patient. Partner with the National Institutes of Health (NIH) and the industry to facilitate testing and development of new MAT treatments.**

  MAT has proven to reduce overdose deaths, retain persons in treatment, decrease use of heroin, reduce relapse, and prevent spread of infectious disease. Expansion of MAT availability for qualified individuals and for short- or long-term treatment is an essential

component of treatment services. Yet approximately 10 percent of conventional drug treatment facilities in the United States provide MAT for opioid use disorder.

Individuals seeking SUD treatment, and even those currently enrolled in a treatment system, often find barriers to using MAT as a component of their treatment. Particularly for populations with opioid use disorders (OUDs) involved in the criminal justice system, there is often inadequate access to FDA-approved medications that are proven to improve outcomes as part of a full continuum of care. Multiple studies have shown that individuals receiving MAT during and after incarceration have lower mortality risk, remain in treatment longer, have fewer positive drug screens, and have lower rates of recidivism than other individuals with OUDs that do not receive MAT. The DOJ, in consultation with HHS and ONDCP, should be directed to increase the use of MAT for OUDs in these correctional settings.

In addition, the Centers for Medicare & Medicaid Services (CMS) should require all federally-qualified health centers (FQHCs) to mandate that their staff physicians, physician assistants, and nurse practitioners possess waivers to prescribe buprenorphine.

There are several barriers to the use of MAT, including a prevalent belief that use of MAT does not constitute true recovery or sobriety. The Federal Government, as a major purchaser of health care services, has a tremendous opportunity to increase the availability of MAT for individuals with OUDs. For example, across the Veterans Administration (VA) and Indian Health Services, there is a lack of providers able to prescribe/administer MAT. For Medicare patients, the Part B physician benefit does not cover methadone treatment and the Part D pharmaceutical benefit does not cover it either, as it is administered by a medical professional. CMS should send a state health official letter requesting that state Medicaid programs cover all FDA-approved MAT drugs for OUD.

Additionally, all FDA-approved MAT should be offered by authorized providers, not just one or two of these approved options. These decisions of which (if any) MAT to be used must be based upon what is best for the patient, not what is best for the provider. This can be mandated by the Executive Branch.

Finally, we urge you to instruct the NIH to begin to immediately work with the pharmaceutical industry in two areas; the development of additional MAT options and the development of new, non-opioid pain relievers based on research to clarify the biology of pain. The nation needs more options to treat those already addicted and can help to prevent addiction in the first place by avoiding the prescription of opioids. The NIH is best positioned, in our opinion, to lead this effort with industry partners.

- **Provide model legislation for states to allow naloxone dispensing via standing orders, as well as requiring the prescribing of naloxone with high-risk opioid prescriptions; we must equip all law enforcement in the United States with naloxone to save lives.**

Naloxone is a lifesaver that rapidly reverses opioid overdose. It is the first line of defense in many parts of our country; if we lose someone to overdose we obviously have no chance to treat them and return them to a productive life. We urge you to mandate, with federal

assistance, that naloxone be in the hands of every law enforcement officer in the United States. By declaring a national emergency, you can empower the HHS Secretary to negotiate reduced pricing for all governmental units. Forty-seven states have expanded access to naloxone in some form. The Federal Government should ensure that naloxone is made available when there is the greatest chance for an overdose. Accordingly, model legislation should include a requirement that naloxone is prescribed in combination with any CDC-defined high-risk opioid being prescribed.

An impediment to naloxone usage and people seeking help in the event of an overdose is the perceived threat of law enforcement involvement. Overly restrictive or punitive laws may prevent the uptake of naloxone or the seeking of aid in an emergency. In response, most state legislatures and some law enforcement agencies have created a variety of immunity and 'Good Samaritan' laws to ensure bystanders and those experiencing an overdose are not deterred from seeking immediate help. States vary widely in the content of 'Good Samaritan' laws, but they generally offer protection to people assisting at the scene of an overdose, or seeking care for their own or another's overdose, from civil or criminal prosecution. As of July 2017, 40 states and the District of Columbia have enacted some form of a 'Good Samaritan' or 911 drug immunity law. In addition to enacting legislation, it is crucial that states ensure the public fully understands the protections provided by the 'Good Samaritan' law and how it empowers them to call 911 in the case of an overdose.

HHS and other federal agencies should be directed by you or your cabinet to make recommendations on ways to identify persons who have overdosed and been revived with naloxone and the feasibility of notification of their primary care and other physicians caring for them. These primary care providers may be prescribing medications that increase future risks of another overdose.

- **Prioritize funding and manpower to the Department of Homeland Security's (DHS) Customs and Border Protection, the DOJ Federal Bureau of Investigation (FBI), and the DEA to quickly develop fentanyl detection sensors and disseminate them to federal, state, local, and tribal law enforcement agencies. Support federal legislation to staunch the flow of deadly synthetic opioids through the U.S. Postal Service (USPS).**

  Illicit fentanyl and fentanyl analogs are the next grave challenge on the opioid front and the awful news is that it is much, much more deadly than hydrocodone, oxycodone or even heroin. Since 2012, the nation has seen an alarming increase in the number of drug overdose deaths that involve fentanyl, a synthetic opioid many times more powerful than heroin, as well as heroin and cocaine laced with non-pharmaceutical fentanyl. Fentanyl defies detection at our borders, as the small quantities involved for psychoactivity of fentanyl and fentanyl analogs challenge Customs and Border Protection, USPS, and express consignment carriers' ability to detect and interdict. We are miserably losing this fight to prevent fentanyl from entering our country and killing our citizens. We are losing this fight predominately through China. This must become a top tier diplomatic issue with the Chinese; American lives are at stake and it threatens our national security. Our inability to reliably detect fentanyl at our land borders and at our international mail handling facilities creates untenable vulnerabilities.

Key federal agencies, including the DEA, DHS, FBI, and DOJ, should coordinate pursuant to the Controlled Substances Act to intercept fentanyl (and other synthetic opioids) in envelopes and packages at mail processing distribution centers, and increase detection efforts using enhanced technology, more manpower, and expanded canine deployment. Only a presidential directive will give this issue the top level attention it deserves from DOJ, DHS, and USPS.

- **Provide federal funding and technical support to states to enhance interstate data sharing among state-based prescription drug monitoring programs (PDMPs) to better track patient-specific prescription data and support regional law enforcement in cases of controlled substance diversion. Ensure federal health care systems, including Veteran's Hospitals, participate in state-based data sharing.**

  PDMPs are state-run electronic databases used to track the prescribing and dispensing of controlled prescription drugs. They are designed to give providers access to critical information regarding a patient's controlled substance prescription history, and can help health professionals identify patients who may be or are at risk of misusing prescription opioids or other prescription drugs. PDMPs are also used by professional licensing boards to identify clinicians with patterns of inappropriate prescribing and dispensing, and to assist law enforcement in cases of controlled substance diversion. Multiple published best practices for utilizing PDMPs, including guidelines from the Heller School for Social Policy and Management at Brandeis University, have identified interstate data sharing among PDMPs as a top priority to ensure that healthcare professionals and law enforcement have a complete picture of prescribing practices and controlled substances diversion. Numerous professional health organizations, including the American Medical Association (AMA) and the Association of State and Territorial Health Officials (ASTHO), agree that PDMPs are an effective and important clinical tool to combat the addiction crisis; however, they are being significantly underutilized in the vast majority of our states. Forty-nine states now have PDMPs but not nearly a majority of those are sharing their information. This is unacceptable. We urge you to direct the VA and HHS to lead an effort to have all state and federal PDMP systems to share information and to set a deadline of July 1, 2018 to achieve this data sharing.

  In addition to sharing data between states and the Federal Government, the PDMP needs to be improved with regard to its ease of use, and inclusion of other data to assist prescribing doctors. Ideally, clinicians should check their state PDMP before making the decision to prescribe either an opioid or benzodiazepine (several states already have this requirement in place), determine whether their patient has had an overdose, and other relevant information that can be summarized into categories of high to low risk.

- **Better align, through regulation, patient privacy laws specific to addiction with the Health Insurance Portability and Accountability Act (HIPAA) to ensure that information about SUDs be made available to medical professionals treating and prescribing medication to a patient. This could be done through the bipartisan Overdose Prevention and Patient Safety Act/Jessie's Law.**

Providers and other advocates have found that certain privacy regulations, while well-intentioned patient protections, act as a barrier to communication between providers, can make it difficult for family members to be involved in a loved one's treatment, and limits the ability to use electronic health records to their full potential. 42 CFR Part 2, which requires addiction treatment professionals to acquire written patient consent before sharing any information with a patient's other health care providers, including when the addiction treatment facility is part of a larger health care system, is a particular hindrance to comprehensive health care. Making it administratively difficult for providers to share information has ill-effects on patients in both physical and behavioral health settings, by restraining physicians' ability to make informed healthcare decisions.

We urge you to direct that regulation be changed to permit the sharing of this type of information among health care providers and the loved ones of those suffering from SUDs. Otherwise, drugs with high abuse liability may be prescribed to people with OUD. That will lead to even more unnecessary and preventable deaths.

- **Enforce the Mental Health Parity and Addiction Equity Act (MHPAEA) with a standardized parity compliance tool to ensure health plans cannot impose less favorable benefits for mental health and substance use diagnoses verses physical health diagnoses.**

  As Congressman Kennedy spoke eloquently about at the first Commission meeting, there has long been a difference in how individuals with health insurance receive treatment and medication for physical health diagnoses versus mental health and SUD diagnoses. The Mental Health Parity and Addiction Equity Act of 2008 (MHPAEA) prohibits health insurance plans that cover behavioral health from imposing benefit limitations on mental health or SUD treatment that are less favorable than limitations imposed on medical or surgical benefits. Benefit limitations can be quantitative, such as visit limits, or non-quantitative, such as pre-authorization requirements. But not providing real parity is already illegal. The Commission urges you to direct the Secretary of Labor to enforce this law aggressively and to penalize the violators.

  The Commission heard from numerous organizations, including ASAM and the American Academy of Addiction Psychiatry, about the need to systematically monitor and enforce MHPAEA with a standardized tool, and actual penalties for non-compliance, to ensure parity in the coverage of mental health and addiction treatment services. The Labor Secretary, with appropriate direction from you, is the person to do this.

  At this point, the largest outstanding issue is treatment limits. Patients seeking addiction treatment, including MAT, are often subjected to dangerous fail-first protocols, a limited provider network, frequent prior authorization requirements, and claim denials without a transparent process. The Commission applauds SAMHSA's work with multidisciplinary teams from states to improve parity enforcement and public education. However, we need robust enforcement of the parity law by the state and federal agencies responsible for implementing the law. Regulators should be required to levy penalties against health plans that violate MHPAEA, and information about parity violations should be made available to the public.

It is not only critical that the Federal Government provide sufficient resources to prevent and combat this disease; it must also provide the easiest pathway for private providers and local and state governments to achieve success.

That is why the Commission, as a primary focus of the final report, is undertaking a full-scale review of federal programs, regulations, laws, and funding mechanisms targeted toward addressing addiction.

In addition to a full review of federal funding and programs and obstacles and opportunities for treatment, the final report will include, but not be limited to, a more thorough examination of the following issues:

- Development of a national prevention strategy using "big data analytics" to devise targeted prevention messages that employ cutting-edge methods of marketing and communications.
- Evidence-based prevention programs for schools, and tools for teachers and parents to enhance youth knowledge of the dangers of drug use, as well as early intervention strategies for children with environmental and individual risk factors (trauma, foster care, adverse childhood experiences (ACEs), and developmental disorders).
- The need for satisfaction with pain level as a satisfaction criteria through which health care providers are evaluated by HHS.
- Workforce access and training needs within the treatment community nationally, with a particular focus on the regions of the country with the highest overdose deaths.
- Improvements in treatment programs, based on adherence to principles of evidence-based treatment, continuum of care, outcome measures, and patient education on quality treatment.
- Research initiatives and opportunities to combat the epidemic and enhance treatment options, including alternative pain management strategies, and treatment for vulnerable populations such as pregnant women, and substance-exposed infants through work by the NIH, HHS, CDC, FDA, SAMHSA, and pharmaceutical partners.
- Opportunities to further the practice of substance use screenings and referrals through CMS quality measures.
- Opportunities for patient protections providing better information about the risks and benefits of taking prescription opioids.
- Supply reduction of heroin, fentanyl analogs and counterfeit pills through coordinated federal and state law enforcement initiatives.
- Targeted data collection and analytics needed to identify most effective prevention and treatment strategies, quality treatment access programs, reimbursements, and aid to law enforcement activities. The possibility of a behavioral health surveillance system run through CDC that tracks prevalence rates, treatment modalities, and comorbidities with other illnesses in real-time.
- Regulatory or statutory changes to reduce commercial insurance barriers to MAT, such as dangerous fail-first protocols and onerous and frequent prior authorization requirements.

In our final report, we will provide an additional set of detailed recommendations that, if implemented, will ensure that the Federal Government operates as a strong partner in the fight against addiction and the opioid crisis.

Finally, our country needs you, Mr. President. We know you care deeply about this issue. We also know that you will use the authority of your office to deal with our nation's problems. The Commission looks forward to submitting its final report.

Sincerely,

Commission members

FENTANYL†

SAFETY RECOMMENDATIONS FOR FIRST RESPONDERS

† For the purposes of this document, fentanyl, related substances, and synthetic opioids (herein after referred to as fentanyl†) includes fentanyl analogues (e.g., acetylfentanyl, acrylfentanyl, carfentanil, furanylfentanyl), novel synthetic opioids (e.g., U-47700), and other drugs that may be laced with these substances.

- **The abuse of drugs containing fentanyl† is killing Americans. Misinformation and inconsistent recommendations regarding fentanyl† have resulted in confusion in the first responder community.**
- You as a first responder (law enforcement, fire, rescue, and emergency medical services (EMS) personnel) are increasingly likely to encounter fentanyl† in your daily activities (e.g., responding to overdose calls, conducting traffic stops, arrests, and searches).
- This document provides scientific, evidence-based recommendations to protect yourself from exposure.

WHAT YOU NEED TO KNOW

- Fentanyl† can be present in a variety of forms (e.g., powder, tablets, capsules, solutions, and rocks).
- Inhalation of airborne powder is MOST LIKELY to lead to harmful effects, but is less likely to occur than skin contact.
- Incidental skin contact may occur during daily activities but is not expected to lead to harmful effects if the contaminated skin is promptly washed off with water.
- Personal Protective Equipment (PPE) is effective in protecting you from exposure.
- Slow breathing or no breathing, drowsiness or unresponsiveness, and constricted or pinpoint pupils are the specific signs consistent with fentanyl† intoxication.
- Naloxone is an effective medication that rapidly reverses the effects of fentanyl†.

Actions to take . . .

To protect yourself from exposure

- Wear **gloves** when the presence of fentanyl† is suspected.
- **AVOID actions that may cause powder to become airborne.**
- Use a properly-fitted, NIOSH-approved **respirator ("mask")**, wear **eye protection**, and minimize skin contact when responding to a situation where small amounts of suspected fentanyl† are visible and may become airborne.
- Follow your department guidelines if the scene involves large amounts of suspected fentanyl† (e.g., distribution/storage facility, pill milling operation, clandestine lab, gross contamination, spill or release).

When exposure occurs

- Prevent further contamination and notify other first responders and dispatch.
- Do not touch your eyes, mouth, nose or any skin after touching any potentially contaminated surface.
- Wash skin thoroughly with cool water, and soap if available. **Do NOT use hand sanitizers as they may enhance absorption.**
- Wash your hands thoroughly after the incident and before eating, drinking, smoking, or using the restroom.
- If you suspect your clothing, shoes, and PPE may be contaminated, follow your department guidelines for decontamination.

If you or other first responders exhibit

- **Slow Breathing or No Breathing**
- **Drowsiness or Unresponsiveness**
- **Constricted or Pinpoint Pupils**

- Move away from the source of exposure and call EMS.
- Administer naloxone according to your department protocols. Multiple doses may be required.
- If naloxone is not available, rescue breathing can be a lifesaving measure until EMS arrives. Use standard basic life support safety precautions (e.g., pocket mask, gloves) to address the exposure risk.
- If needed, initiate CPR until EMS arrives.

Collaborative Support From:

- American College of Emergency Physicians
- American College of Medical Toxicologists
- American Industrial Hygiene Association
- Association of State and Territorial Health Officials
- Association of State Criminal Investigative Agencies
- Fraternal Order of Police
- International Association of Chiefs of Police
- International Association of Fire Chiefs
- International Association of Fire Fighters
- Major Cities Chiefs Association
- Major County Sheriffs of America
- National Alliance of State Drug Enforcement Agencies
- National Association of Counties
- National Association of County and City Health Officials
- National Association of Emergency Medical Technicians
- National Association of EMS Physicians
- National Association of State EMS Officials
- National Governor's Association
- National HIDTA Directors Association
- National Narcotic Officers' Associations' Coalition
- National Sheriffs' Association
- National Volunteer Fire Council
- Police Executive Research Forum
- Police Foundation

https://www.whitehouse.gov/ondcp/key-issues/fentanyl

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